A

# COMPEND

OF

# PATHOLOGY

## GENERAL AND SPECIAL.

A STUDENTS' MANUAL IN ONE VOLUME


BY

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**SECOND EDITION,**

CONTAINING 131 ILLUSTRATIONS.

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# PREFACE.

THE two Compends of Pathology by the same author, issued in 1902, are here presented in a second edition as one volume. A chapter on the Nervous System and several illustrations have been added, and the text has been thoroughly revised.

The effort has been to present the subject clearly, with sufficient completeness for the students' needs, and, as before, controversial matter and references to authorities have been left out.

It is hoped that the book in its new form may be found a useful guide to an important subject.

A. E. T.

Cornell University
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November, 1903.

# TABLE OF CONTENTS.

## PART I.—GENERAL.

### CHAPTER I.



### CHAPTER II.



### CHAPTER III.

## CHAPTER IV.



## CHAPTER V.

## CHAPTER VI.

## CHAPTER VII.

## CHAPTER VIII.



## CHAPTER IX.



## CHAPTER X.

## CHAPTER XI.

## CHAPTER XII.



# PART II.—SPECIAL.

## CHAPTER XIII.

## CHAPTER XIV.

## CHAPTER XV.

## CHAPTER XVI.

## CHAPTER XVII.



## CHAPTER XVIII.

## CHAPTER XIX.

## CHAPTER XX.

## CHAPTER XXI.

## CHAPTER XXII.



## CHAPTER XXIII.

# LIST OF ILLUSTRATIONS.

# COMPEND OF PATHOLOGY.

## PART I. GENERAL PATHOLOGY.

### CHAPTER I.

### DISEASE IN GENERAL; ETIOLOGY.

**Pathology** is the science which treats of diseases, their causes, nature, signs, process, structural changes and results. It may be broadly divided into Plant and Animal Pathology; the latter comprises Human Pathology, the subject of this work, and Animal Pathology which is a similar study of disease in animals. When the results of Animal and Human Pathology are studied as mutually interpretive it is called Comparative Pathology, a field still imperfectly developed. Some of the subdivisions of Pathology are so important to the physician that they are treated as separate branches, under the head of Symptomatology, Diagnosis, etc.; but strictly these belong to Pathology and they are easy to comprehend in proportion as one is familiar with Pathology in the narrow sense.

**Human Pathology** is divided into General and Special. The former considers processes or their results common to all or many forms of disease, and the latter such as are found in any one disease; thus inflammation affects many different organs and diseases and belongs in General Pathology, while syringomyelia belongs only in a special organ, the spinal cord, and that special affection of it. Further subdivisions of Pathology are Gross, treating of the naked-eye appearances of

diseased organs and the technique of postmortem examinations; Microscopic, or Histo-pathology, the study of such organs by the microscope and the technique implied in such study; Clinical, the examination of blood and discharges for the purpose of clinical diagnosis; Morbid Function, called also Pathological Physiology; Pathochemistry, etc.

**Disease** is that condition of an organism in which there is any departure from the normal in function, structure or relation; it may be local or general, and tends to recovery or death.

**Death** is that condition of an organism in which further metabolism is impossible. It may be local or general and if local is called by the special names, gangrene, necrosis, caries, etc. This definition excludes cases of suspended animation or function, for in the proper conditions metabolism is still possible; thus a portion of the organism may be frozen and apparently dead, and yet recover.

**Etiology** is the branch of pathology which considers the causes of disease. These may be *predisposing* or *exciting*, diminishing the resistance to disease or actually beginning it. *Predisposing causes* often become exciting by their relative severity. Among the common predisposing causes may be mentioned defective nourishment in utero; premature birth and consequent feebleness from the start; deficient food, oxygen and pure water; bad sanitary conditions; extreme changes in heat and atmospheric pressure; great humidity, especially with extreme temperature; heredity, whose importance is less than has been taught formerly; bodily and mental fatigue, starvation (up to the loss of about 33 per cent. of body weight), excessive bodily discharges, as of sweat and urine — any of these, alone or in combination, may predispose to disease, or beyond a certain degree actually excite it. *Exciting causes* are frequently injuries, extreme heat or cold suddenly applied, poisons developed in the body or taken in from without, parasites, including microörganisms. Certain diseases are almost

wholly mechanical, as when valve defects in the heart produce chronic passive hyperemia in the liver; others are especially chemical in their nature, as seen in bacterial invasions and consequent toxemia. More than one disease may exist in the same patient, and at times it is apparent that one is primary and the others are secondary;—thus inflammation of the lung spreads to the pleura, malignant disease of the stomach sets up similar changes in the liver, or obstacles in the lesser circulation cause passive hyperemia of the central veins of the liver with pressure atrophy of the hepatic cells, or a stone in the pelvis of the kidney descends and becomes a vesical calculus, or failure of the renal elimination causes colitis through the effort of the solitary glands in the colon to assume the duty.

*Injuries* may act suddenly, as in the case of blows or stabs; or slowly by lessening the space an organ ought to occupy, as when pleural exudate crowds a lung into a condition of atelectasis; or as a repetition of slight mechanical attritions, as seen in various trades where the use of a tool causes excessive development of the local epidermis. The results of injury are called contusion, wound, fracture, concussion, etc. Their usual common feature is tissue destruction and nerve irritation, which cause disorder of circulation, or inflammation, or perverted growth of cells.

Effects of heat and cold are strictly injuries but are usually considered by themselves. *Local excess of heat* causes relaxation of vessels, exudation of serum and blood, and finally charring, the effect depending on intensity and duration of cause; hyperemia, vesiculation, charring, and complete destruction being the so-called surgical degrees of burns. This grouping neglects the constitutional effects, which are important according to the amount of tissue burned, a burn of one-third of the body surface usually causing death. The fatal result is explained by loss of function of skin, nervous shock, destruction of blood cells and plasma, toxic substances formed

in the blood or absorbed from the burned surface, secondary intense internal congestion especially of the alimentary mucous membrane and perhaps embolism from small vessels thrombosed by the heat. General excessively high temperature causes heat stroke, insolation, or heat exhaustion, with increased respiration and pulse rate, sweating, cerebral hyperemia and edema, and death from the latter or from albuminous coagulation throughout the body.

*Extreme cold* has somewhat similar effects, leading to local or general death if severe and prolonged. Applied for a short time cold produces reflex vasomotor disturbances recognized under the popular term "catching cold." Either extreme of temperature is worse if associated with moisture.

*Barometric pressure,* if diminished as in mountain and balloon ascensions, or increased as in diving and caissons, may cause bleedings, drowsiness, ataxic gait, vomiting, delirium and even various paralyses.

*Electric currents,* either as lightning stroke, or from a dynamo, may cause burns of the integument, often curiously distributed over the surface, and injuries to the nervous system or to other organs.

**Poisons.**—Any substance is called a poison which will cause injury or death otherwise than mechanically, when introduced into the body in relatively small amount. It may be either vegetable, mineral, or gaseous in origin. Grouped according to their action in the organism poisons are:

Irritants, including pure irritants, not chemically destructive, as arsenic; corrosives, destroying tissue, as mineral acids; and neurotics, acting on nervous system.

The latter include simple narcotics, as opium; acronarcotics, with strong irritating action, as aconite and strychnine; septics, derived from albuminous decay and acting through destruction of the blood.

**Auto-intoxication.**—It is a law that any organism is self-destructive if compelled to reabsorb the waste products of its own metabolism, and to this the human being is no exception. He may poison himself by means of any of his excreta, and to the special form of this which is due to putrefaction within the alimentary canal the name auto-intoxication has been given. This and allied forms will be treated in Chaps. IV.-V., while the effects of introduced poisons will be considered in Part II., p. 685.

Various circumstances affect the action of poisons of either of the classes cited above. Thus, a poison like carbolic acid, if introduced in concentrated form into the empty stomach, may cause death instantaneously by shock, or secondarily by its action on the alimentary mucous membrane, while, if dilute before ingestion or mixed with stomach contents, there may be time for absorption and general effects as well as the local reaction. In the one case the esophagus and fundus of the stomach may be the seat of its action, in the other the acid may ride over the stomach contents and affect the pylorus or the duodenum alone. Again, a patient who has been taking a drug and thus acquired a tolerance for it may resist a dose which would prove fatal in another. Too large a dose may cause vomiting and prevent a fatal result, while less may cause death at once or after an appreciable interval. Many poisons, if given in small amounts, may set up secondary tissue changes, which mask the action of the poison and hence are fatal indirectly, as in chronic arsenic and mercurial poisoning.

The action of poisons in general may impair the blood in its cells or plasma, or modify the organs, or inhibit function without producing gross anatomical change.

**Blood Poisons.**—The *blood poisons* are either liquid and volatile or gaseous, or they may be solid matters held in suspension by tissue juices and absorbed from wounds or the intestine, or introduced directly into the blood-channels. They may prevent the exchange of gases in the blood by making a

combination with the hemoglobin which is stronger than that with atmospheric oxygen, of which the standard and commonest is carbon monoxide (illuminating gas poisoning), death then being due to an asphyxia generalized throughout the tissues; or they may alter the hemoglobin after the red cells are affected, as is seen in the cyanosis following the administration of many coal-tar derivatives; or they may cause tissue changes in addition, as in the case of ricin (from *Ricinus communis*); or they may affect the plasma, increasing its tendency to coagulate and thus producing thrombosis, as is the case with albumose, carbon dioxide, and a few others.

**Corrosive Poisons.**—*Poisons which cause tissue changes* as their chief effect usually attack the parts with which they are in contact, as the alimentary mucous membrane and the skin. The typical examples of this action are furnished by strong acids and alkalies, which abstract water from the part, coagulate its albumins, form soapy or gelatinous compounds with its elements, etc. Frequently there is a pronounced and characteristic alteration in the color of the part, as in the yellow of nitric acid poisoning and the black of sulphuric. All degrees of effect may be found from simple redness or inflammation to necrosis and sloughing. Such poisons are usually called caustic or corrosive. A special case of the corrosive poisons is found in the irritant gases and volatile compounds which attack the conjunctiva and the respiratory mucous membrane; examples are ammonia, formaldehyde, chlorine and bromine. These may cause edema or inflammation of the parts mentioned. Other poisons of this class act both locally and at a distance, like carbolic acid which causes a white eschar of the gastric mucous membrane, with rigidity of the rugæ, and also acute inflammations of the organs which excrete it, the kidneys. Mercury bichloride, cantharidin, and to a certain extent phosphorus and arsenic also belong in this group.

**Nerve Poisons.**—Among the poisons which cause death without appreciable tissue change, hence called heart or nerve

poisons, may be mentioned alcohol, amanita muscaria, strychnine, atropine and many other alkaloids. In large doses they act immediately upon the centers for respiration and circulation, or the cord, or the cardiac muscle and ganglia, and are rapidly fatal; in smaller and frequent doses they may cause degeneration in the nervous tissues and consequent paralysis.

Disease caused by parasites, and by that special division of these known as microörganisms, will be treated in Chapters VIII. and IX.

**Foreign Bodies.**—A further cause of disease may be found in the introduction of lifeless foreign bodies into the organism. Good examples of this are fatty embolism of the capillaries after fractures, air in the veins, foreign bodies in the larynx and trachea, all of which mechanically interfere with the function of lungs or heart; bits of catheters or other substances in the bladder which may form the nuclei of large calculi. Beside their mechanical effects such foreign bodies may irritate the tissues and cause inflammation or deprive a part of its nutrition and cause atrophy.

Though one or more of the causes mentioned may excite disease, yet the peculiar results of such action vary within wide limits, being modified as to time (acute, subacute and chronic disease), by the age and condition and sex of the patient, by previous or intercurrent attacks of another nature, by tendencies to rhythmic cycles in the disease itself and many other and more obscure influences.

## CHAPTER II.

### DISORDERS OF DEVELOPMENT; TERATOLOGY.

UPON the developing embryo we may suppose that two sets of influences are acting, which we must be content to name without understanding. The first is the innate self-developing power of the embryo, and the other is complex, derived from the maternal structures as uterus, blood and nerves, and, to an extent increasing with growth, from the outside world. In proportion as the balance between these influences is disturbed the fetal parts are imperfectly developed, making malformations if slight and monsters if more pronounced; a fairly accurate distinction between them being that the malformation may be produced late in fetal life and not be incompatible with extra-uterine existence, while the monstrosity usually results from very early interference with the growth process and if extreme renders the child non-viable.

**Congenital Abnormality.**—Congenital departures from the normal are usually divided into single and double anomalies and may result from internal or external causes. As due to internal causes we consider all variations from the type, which if persistent would tend to make new species, and partly explain them by assuming some abnormality in either the male or the female element, or some incompatibility between them, perhaps essentially a question of physiological chemistry. When the variation appears in parent and child we speak of inherited abnormalities, as seen in the frequent occurrence of extra teeth and digits in immediately succeeding generations, and the prevalence of certain diseases in a family where we suppose the existence of some bodily peculiarity to account for it;

if the abnormality skip a generation or two we speak of its later appearance as atavism.

*External causes* of variation, that is, external to the developing embryo, may be injury to maternal or fetal tissues, from jarring or pressure, disordered supply of nutrition (including oxygen), powerful nervous influences from the mother, and the actual transmision of disease from her to the child.

When the variation occurs in different cases with about the same characteristics we speak of it as *typical,* an instance of which would be hairlip and club-foot; where it is entirely anomalous we call it *atypical.* The former are usually to be referred to internal and the latter to external causes.

**Varieties of Congenital Malformation.**—Among the single forms of congenital abnormality may be mentioned those due to

1. Defective or arrested growth, hypoplasia or aplasia: Example, dwarfing, absent limb or brain or small size in either; non-closure of parts, often in the middle line, causing clefts; adhesion of adjacent parts, as horseshoe kidneys.

2. Excess of growth and development; as giant size of a part, extra breasts, digits, hair, etc.

3. Wrong disposition of parts; dexiocardia.

4. Tissues in the wrong place, or fetal tissues persistent; causing heterotopous and heterochronous growths. (See Tumors, Chap. VII.)

5. Sex anomalies, true and false hermaphrodism. The embryo, potentially bisexual, normally develops one set of organs to the disadvantage of the other; variation here implies marked development of the subsidiary set of organs, which is common in slight degrees. Complete formation of both, true hermaphrodism, is so rare that its existence has been denied.

**Monstrosity.**—True monstrosity is more common in the double forms and may appear as duplication of any part of the fetus or complete doubling, the twins being closely connected at some part; they are always of the same sex, usually

joined at corresponding parts, as head, thorax or sacrum, and may be of equal size or of all degrees of inequality. In one sense twin and triple births of separate children are abnormal, being reversions from the typical human single birth to the lower animal multiple, but a pathological monstrosity does not appear unless the twins are fused in greater or less degree. These double forms arise from a single ovum and germ vesicle and imply doubling of the embryonic area in a single blastodermic vesicle, with later coalescence, perhaps due to the entrance of two spermatozoa through the same micropyle; or two primitive streaks and medullary grooves, which may blend; or a medullary groove partly or wholly double; or a multiplication of parts late in fetal life. The first three explain abnormalities in the parts of the main somatic axis, the variations of the latter kind lie outside.

Common Anomalies.—Adequate treatment of the subject of teratology is impossible in a compend of this size; all that can be done is to mention the commonest anomalies. See also the various organs in Part II.

The Heart may be deficient in part of the septum, making an organ of two chambers, like the fish's heart, or of two auricles and one ventricle, like the reptilian type; or one or more valves may be defective or redundant, stenosed or dilated; or fetal channels may persist, with general cyanosis as the result; or the aorta may be hypoplastic, with imperfect development of the lower half of the body; or the entire heart and main blood channels may be transposed.

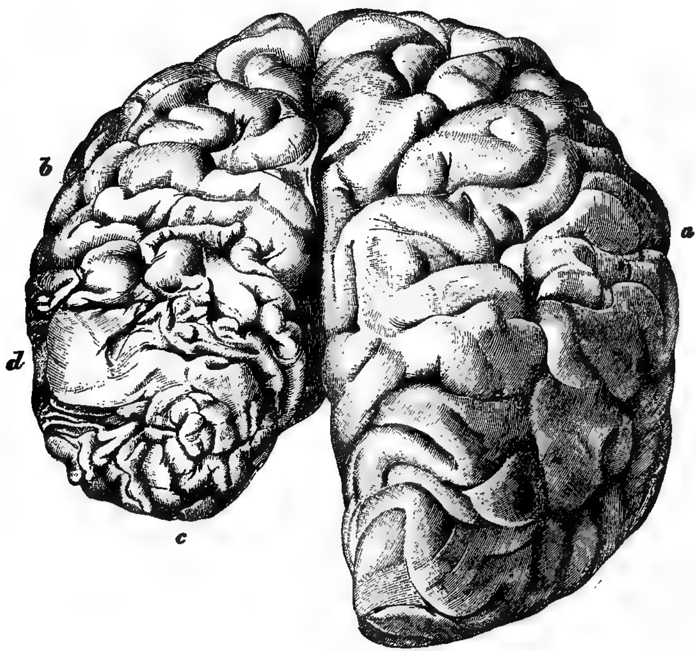
The Lungs and Liver seldom show important abnormalities. They may have fewer or more lobes, thus the right lung may have two or four and the liver may have four; the liver may also present vertical furrows on its superior aspect, which are often congenital and have received the name of Zenker's furrows.

The Kidneys often show the remains of fetal lobulation. They may be united at the lower poles by renal or fibrous

tissue, or one organ may be so small as to be functionally inactive, the other being correspondingly large.

The Alimentary Canal shows imperfect closures at the oral end, usually along the line of the premaxillary suture, involving only the lip and then called harelip or running through the roof of the mouth also and known as cleft palate; remains of the omphalo-mesenteric duct, known as Meckel's diverticulum, a small pouch from the free aspect of the ileum about three feet above the ileo-cecal valve, free at its distal end or connected with the umbilicus by a fibrous cord or an open channel; hernias in various situations, which are not due to

FIG. 1.




HYPOPLASIA CEREBRI. (*Ziegler.*)

*a*, Right hemisphere; *b*, left hemisphere; *c*, left occipital lobe, showing microgyria; *d*, fluid collection covered by membrane, region of temporal lobe. From a deaf mute.

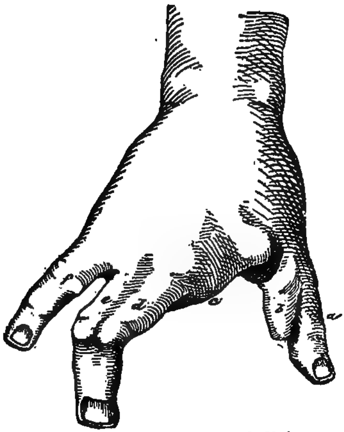
defect in the canal but rather to incomplete abdominal walls; various degrees of imperforate anus, due to imperfect involution of the integument to meet the hind gut.

**The External Genitalia** may be malformed from non-union of parts in the median line, causing epispadias and hypospadias in the male, marked degrees of which sometimes pass for hermaphrodism, extroversion of the bladder in either sex, bicorn uterus and double vagina in the female.

**The Nervous System** may present anomalies of the organs or of the enclosing canals or of both. If the neural groove fail to complete its posterior half the spinal cord is exposed, making spina bifida in its varying degrees, or the nervous tissue may be represented by rudimentary and imperfect nerve strands and ganglia. Frequently the defect of the canal allows the contents to escape, making syringo-myelocele if the central canal of the cord is dilated, myelo-meningocele if the hernia is from the neural canal alone, encephalocele if from the cranium and containing brain tissue, encephalo-meningocele containing brain and fluid, meningocele if containing fluid alone. In all these cases there is a tumor connected with the spinal column, usually presenting posteriorly through the imperfect bony arches, lined more or less completely by dura and pia with or without nervous tissue, and containing varying amounts of cerebro-spinal fluid. The most pronounced degree presents a shallow groove (the posterior half entirely absent), with no brain or cord (anencephalia and amyelia), but such monsters are incapable of independent existence and are of only scientific interest. Defects arising after the spinal canal and cranium are formed lead to small brain and cord (micrencephalia and micromyelia), small or absent convolutions; clefts or depression in the cortex, the place being filled by excess of fluid (porencephalia); similar excess of fluid within the ventricles or over the cortex, known as congenital hydrocephalus.

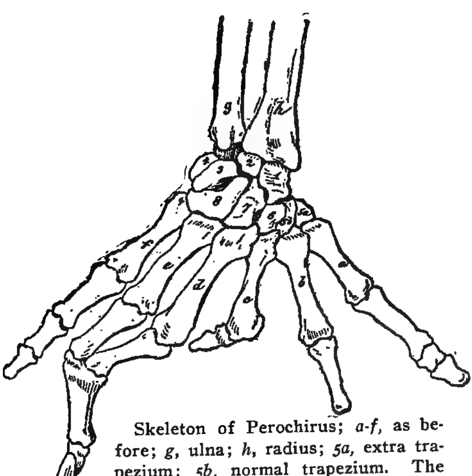
**The Skeleton** presents absent, deformed, and imperfect bones, often traceable to pressure during fetal life; the limbs

FIG. 2A.



Perochirus with fusion of digits; *a*, extra thumb; *b*, normal thumb; *c*, index finger. *d-f*, the other three fingers.

FIG. 2B.



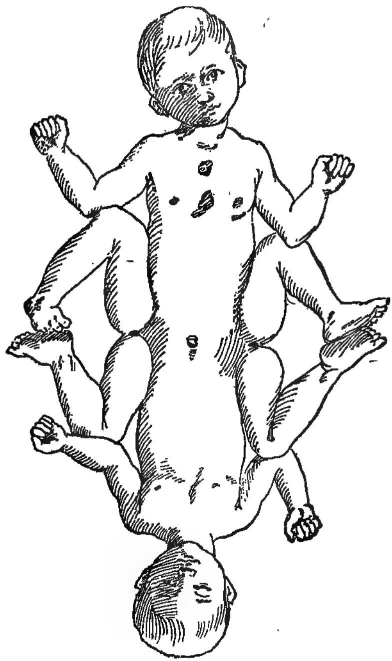
Skeleton of Perochirus; *a-f*, as before; *g*, ulna; *h*, radius; *5a*, extra trapezium; *5b*, normal trapezium. The other figures refer to normal carpal bones.

may be absent from non-development, or from intra-uterine amputation by amniotic bands, or variously blended, and redundant in the double forms. The digits are frequently increased or diminished in number and variously misshapen; extra digits are often associated with extra teeth and show strong heredity.

**Double Monsters** are of two main varieties; either the twins are of the same size and degree of development, or there is marked discrepancy between them. Instances of the first kind may be capable of extra-uterine life; the same is sometimes true of the second variety. They are named in the first variety by adding to the part by which they are joined the syllable pagus (from radicle *pag*, meaning to fasten). Thus a pair of twins joined by the thorax are called thoracopagus; if by the heads, ceph-

alopagus; if by buttocks, ischiopagus. These forms frequently have their internal organs so separate and well developed that their association is little more than an inconvenience. When

FIG. 3.



ISCHIOPAGUS. (*Ziegler.*)

one of the twins is much larger than the other it is called the autosite and the smaller is the parasite; the latter is usually very imperfect in some important region or organ.

# CHAPTER III.

## DISORDERED BLOOD-SUPPLY.

**Normal Circulation.**—The circulation is divided into the greater and the less, or the systemic and the pulmonary, and the conditions in the two are not identical. The blood flow through the systemic and larger division depends upon five factors: The active contractions of the left auricle and ventricle; the arterial recoil, especially marked in the aorta and its main branches; the caliber of the arteries and arterioles, dependent in great part upon vasomotor influence; passive compression of the veins by the muscles among which they lie; and the inspiratory hiatus which determines blood from the large venous trunks toward the right side of the heart. Interference with any of these may cause local or general disturbance of the circulation. A subsidiary department of the systematic circulation in which disorders are common is the group of veins known as the portal, which from their anatomical relations offer many peculiarities. The flow through the lesser circulation is due chiefly to the activity of the right auricle and ventricle, aided by the movements of the thorax and the difference in pressure between the two circulations. The blood-pressure is high in the aorta, owing to the elasticity of its walls and the resistance of the countless subdivisious of the arterial tree; in the capillaries it is less and in the veins, except when gravity acts upon a long column of blood, it is very low:—normally it is least in the pulmonary circulation. As there is no method of accurately measuring the

pressue in the capillaries we can say merely that it must vary according to the conditions in the arteries and the veins; if the arterial supply increases without change in the veins, it must rise, and *vice versa.*

**Causes of Variation.**—*Disorders of circulation* may be local or general, and are the result of many and varied causes. Alterations in cardiac function may be either muscular or valvular. If muscular we may have *excessive* or *diminished* action. Over-action is less common than its opposite, and usually temporary; it raises the blood-pressure, the quantity of blood in the vessels and the rate of flow; if the vessel be diseased these may combine to produce hemorrhage. Such increase of frequency and force in the heart's action may be due to emotion, muscular action or drugs, in all of which it is usually temporary. With habitual excess in eating and drinking overaction becomes chronic, with hypertrophy of the heart, bounding pulse and flushed face. In certain diseases, as exophthalmic goitre, there is tachycardia with consequent hypertrophy of the left ventricle. Slight degrees of increased action lead to heightened glandular and mental activity; if prolonged, to headache and insomnia.

*Diminished power and frequency* in the cardiac function are common and important in results. By certain drugs, of which digitalis is the typical example, the frequency may be lessened while the power increases, but as a pathological condition we usually find both force and frequency decreased. This may be due to fatigue of the muscle fibers from overaction, or be a result of high fever, poison of various kinds, starvation and anemia, or follow changes in the coronary arteries. These and other causes may lead to degeneration of the heart muscle, the cells being cloudy or fatty, or holding pigment, or in great part replaced by new connective tissue. When the coronary arteries are at fault, we may find atheromatous plates in them, narrowed caliber and degenerative changes in the territory of distribution. Such weakened action is frequent with

valvular lesions, pericardial effusion and adhesions, new growths of heart and lungs, vesicular emphysema, cardiac thrombosis, etc. Whichever valve is involved, or however the heart may be weakened, the result is an abnormal collection of the blood in the lungs; with lesions in the left side of the heart the blood is dammed back through the mitral and into the lungs, if on the right side, the chief agent for the pulmonary circulation is eliminated with the production of pulmonary congestion. If the left side alone is involved, the right remaining vigorous, the venous congestion is not systemic; as soon as the right ventricle becomes weak also, there is general passive venous hyperemia. As results we find that the arterial pressure falls, the circulation is slowed, nutrition throughout suffers, with cyanosis, edema, cold extremities, etc. The pulse wave is weak and slow, and if the heart acts slowly enough the arterial system has time between beats to nearly empty itself from the arterial recoil.

**Valve Changes.**—The disorder of the heart function may begin as a valvular lesion and any one or more of the four valves may be affected, in the order of frequency, mitral, aortic, tricuspid and pulmonary; in time the muscular tissue is always involved also. As far as the circulation is concerned the result is passive venous hyperemia. (See p. 346.)

*Vasomotor Phenomena.*—The caliber of the smaller vessels is controlled partly from cerebral centers in medulla and pons, the fibers passing down the cord and out through the anterior nerve roots to the sympathetic, and partly from centers distributed along the cord. Anemia of the nervous tissue, especially of the medulla, and highly venous conditions of the blood cause increased activity of these vasomotor centers, general vasoconstrictor action and acceleration of the blood flow. Their activity is heightened by some afferent impulses, with a rise in the blood-pressure, and depressed by others, when pressure falls: local effects of stimulus are frequently made up of both these phenomena, a constriction with anemia fol-

lowed by a dilatation and hyperemia, or vice versa. The mechanism in the region of face and head is very much under the control of the emotions, as seen in blushing, and in anger of the red and the pale forms. Certain toxic actions, from poisons introduced or manufactured in the body, as in the coma of alcoholism and of uremia, may be associated with profound vasomotor effects, with corresponding pallor or flushing of the face and injection of the conjunctivæ. In scarlet fever it is not uncommon to see the entire bodily surface a brilliant red color and the face absolutely pale, the two representing the extremes of vasomotor action. In nearly every irritation it is usual to have a strong constriction followed by a marked dilatation, as seen in holding a piece of ice, the hand being first cold and anemic and then red and hot and hyperemic (similar changes occur in the other hand). This explains why eating snow and ice will not quench thirst, the subsequent hyperemia of the throat aggravating the condition. In the beginning of most inflammations there is first a constrictor effect with hurried circulation and then a dilated condition, with hyperemia, pulsation, subjective throbbing and increased temperature; of the two the second, or dilatation, lasts the longer.

There is a well-developed compensatory mechanism between one region of the body and another by means of this vasomotor circle, of the greatest importance in defence of the body and in disease processes. Thus a scald or burn of the surface may cause vasodilator effects along the alimentary canal, which may lead only to increased functional activity of the mucous membrane or to ecchymosis and subsequent digestion of the part involved, with the production of an ulcer. Severe pain and extremes of mental emotion may lead to such dilatation of the abdominal vascular region that it will contain the greater part of the total blood, with consequent cerebral anemia. This produces syncope and prevents death from excess of pain, or, if of higher degree, causes

it by intravascular hemorrhage, the patient bleeding to death into his own portal system. After injuries to the genital organs and operations about the pelvis this condition of shock is fairly common. Some of these vasomotor effects are physiological and compensatory, as when one of a pair of organs is incapacitated and the blood-supply of the other rises with the necessity for increased function; certain of them are only pathological, as when the inhalation of $CO_2$ causes general contraction of the arterioles, increased blood-pressure, lessened heart activity and venous congestion. In skin disease vasomotor effects are of prime importance, *e. g.*, herpes, urticaria and erythema, the rose rash of primary syphilis and other exanthemata.

**Volume Changes.** *General Hyperemia and Anemia.*—Increase in the total volume of the blood is possible by salt infusion and by transfusion, mediate or immediate, but it seldom persists for any long time, for the renal, sweat and other glands eliminate it very fast, and any excess may be temporarily stored by means of vasodilatation, usually in the abdominal region. Where excess in food and drink is habitual, we may find the condition known as plethora, with resulting cardiac hypertrophy (left ventricle), flushed face, general obesity, and hyperemia of the cerebrum, evidenced by headache and bad temper. A decrease in the total volume, general anemia, is also most commonly temporary, and is seen after loss of blood; if large, this may cause death by cerebral anemia; if smaller in amount, the deficiency is soon made up by absorption of fluid from the tissues, decreased excretion and increase in fluids ingested. This variety of anemia, to be distinguished from essential anemias of every grade (Part II., p 371), is accompanied by lower pressure and pulse rate, and, if persistent, by imperfect filling of the arteries, cardiac atrophy, dry skin, emaciation and torpor, as seen in starvation and those forms of it called cachexia. When the total amount of blood is diminished it is called *oligemia;* when the fluid part is chiefly affected

it is said to be *anhydremia.* The capacity of the venous system is normally far greater than that of the arterial, but from hypoplasia of the arteries this disproportion may exceed the usual limits, and there is then a relative anemia on the arterial side throughout life, with corresponding ill-development of part of the body, usually of all below the umbilicus. Imperfectly developed arteries, disease of the intima, rigidity of the vessel walls, arterio-fibrosis, as seen in kidney disease, aortic stenosis and aneurysm, all may cause increased resistance in the arteries and consequent diminution of their blood capacity and anemia on that side of the circulation. Similarly, vascular dilatation in the arteries may increase the amount of blood in them, lessening the disproportion between arterial and venous capacity and depriving the venous current of its normal *vis a tergo,* tending to general stasis and death.

In the lesser circulation deformities of the thorax, thickened and adherent pleura, effusions into the pleural cavities and vesicular emphysema tend to increase intra-vascular pressure and hence also the effort of the right side to empty itself in systole, producing work-hypertrophy of the ventricle, regurgitation through the tricuspid and dilatation of the auricle. Occasionally such mechanical obstacles in the thorax cause backing up of the blood into the main venous channels, venous pulse in the neck, cyanosis and visceral hyperemia.

*Local Hyperemia, Active.*—Any portion of the body may have within it more than the physiological allowance of blood; the condition is called hyperemia and may be arterial and active or venous and passive. In health no part of the body contains its entire capacity of blood, but physiological activity is associated with and dependent upon increased supply due to vaso-dilator action in the afferent arteries, to be followed by constriction and relative anemia, the entire cycle marked by a rhythm peculiar to the special organ or part. Increased persistent physiological hyperemia may pass the bounds of the normal and sometimes depends upon loss of function in a

neighboring part, as in one of a pair of organs. Excessive stimulation of the vasò-constrictor fibers, active stimulation of the vaso-dilators, and injury of the vascular muscle fibers, all have in the end the same effect of causing active hyperemia, which explains many contradictory drug actions through paralysis by overstimulation. Sudden removal of support may cause active hyperemia in the vessels of various parts, as when a large amount of residual urine is incautiously withdrawn and hemorrhage follows from the vessels which had become accustomed to its pressure. So also the relief of pressure anemia is followed by hyperemia, as when a tight shoe by its removal allows the part to be filled by blood, with consequent growth of the corn which is the joint result of intermittent pressure and blood supply.

Whatever the cause, the signs of active hyperemia are bright red color, slight swelling, subjective warmth and throbbing, local rise of temperature, with perhaps discomfort and pain; the function of parenchymatous organs is increased, muscular power of work is increased with hypertrophy of substance, mental activity may rise or there may be headache or insomnia, excitement, and delirium. The tendency of active hyperemia is first to hypertrophy of the part and second to inflammation. Temporary active hyperemia may leave no postmortem evidences, except where the circulation is peculiar, as in the kidney.

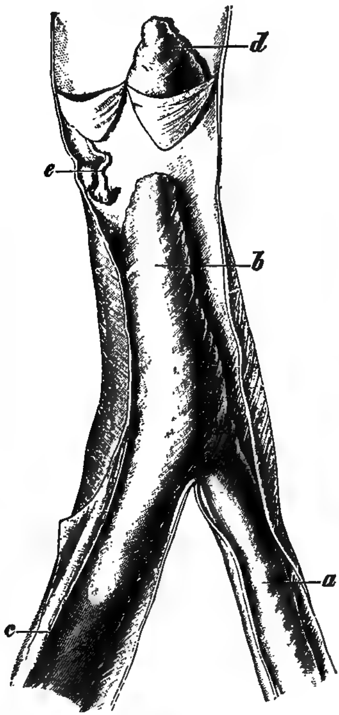
*Local Hyperemia, Passive.*—This is due to imperfect emptying of veins, capillaries and smallest arteries. It may be caused by pressure on a large venous trunk, as by a tumor, dislocated bone, the gravid uterus, or by thrombosis of veins. It is often aided by gravity and the mechanical disposition of the part affected, as in the hyperemia of dependent parts of the lungs in feeble patients. The causes may be more general, as cardiac valvular lesions with partial arrest of arterial circulation and regurgitation of venous blood, obstacles in the lesser circulation, as emphysema, or extra intrathoracic pressure as from

violent muscular exertion, playing wind instruments, etc. When chiefly mechanical and due to gravity it is called hypostatic. In its highest degree venous hyperemia is known as *stasis*, the circulation through the part being nearly or entirely inhibited. The signs of venous hyperemia, especially marked when local, are bluish or cyanotic color of the surface, swelling and edema, lowered function and temperature, and a tendency on the part of the blood to escape from the vessel, the fluid exuding first, then the white cells and lastly the red. If persistent and not too marked, venous hyperemia is followed by degeneration of the higher cells of the part and replacement by new connective tissue, simply because connective tissue, historically among the first evolved, is the only tissue of low enough vitality to thrive in such unfavorable conditions, in which highly specialized cells of more recent acquisition and more sensitive nature, undergo fatty degeneration. In higher degrees the entire nutrition of the part suffers and there is necrosis and gangrene. The new formation of connective tissue is sometimes mentioned as a productive inflammation, but strictly it is a connective tissue replacement and to be regarded as an effort toward repair. When the part recovers from the hyperemia, especially if it has lasted a long time, the cells in the neighborhood and the adjacent lymph nodes may contain a large amount of pigment.

*Local Anemia.*—An active local anemia might be described, being a vaso-constrictor effect and usually without pathological significance. Distinguished from that, any other local anemia might be regarded as passive, if caused by faulty distribution of the blood, as in shock, weak heart, atheroma, thrombosis and aneurysm of an artery shutting off its blood, or pressure on the artery by organizing connective tissue or tumor. Certain drugs, as ergot, and certain nervous influences may also cause a local anemia. If a collateral circulation develops soon there may be no permanent results, but in some arteries, known as end arteries, the only collateral circulation may be

through capillaries and very slow in developing. From the disturbance of pressure in local vein and artery there may be regurgitation of blood through the veins, stasis in the part and a red infarct; without such regurgitation a white infarct may

FIG. 4.




OBLITERATING THROMBOSIS OF FEMORAL AND SAPHENOUS VEINS. (*Ziegler.*)
*a-b*, main thrombus, mixed and laminated; *c*, secondary peripheral red thrombus; *d*, valve with protruding thrombus.

form. Pallor, low temperature and loss of function are the direct results; degeneration, atrophy, or dry gangrene may be the ultimate.

*Stasis.*—When the circulation of a part is nearly or quite at a standstill the blood has the venous character and soon

undergoes changes; the watery part oozes out of the capillaries, the cells partly wander out and partly fuse into a homogenous mass; such changes are frequent in areas of inflammation and special microörganisms seem to have a peculiar power to produce them. They may follow exposure of serous membranes to the atmosphere, too long applications of heat and cold, especially if with moisture, and also action of certain acids and alkalies. Three factors enter into the local effects, the pressure within the vessels and in the tissues, the impaired nutrition of the part and the failure to remove the katabolic products of the cells. The results are seen as edema, diapedesis and hemorrhage, loss of function, atrophy and degeneration of higher cells, coagulation, necrosis and gangrene. The cells undergo simple solution or fragmentation, in some cases with necrosis of the capillary wall and then of the tissue, with or without thrombosis in the veins.

**Thrombosis.**—Clotting of blood occurs in the heart and vessels as a regular postmortem change in the great majority of dead bodies, and the change resembles those observed in blood drawn during life and examined through several hours in a glass. The mass of red fluid separates into two parts; one, the serum, yellow in color, holds the water, salts and albumin which were in the blood, the other, the clot or coagulum, is made up of red cells, white cells and fibrin. On false analogy the production of a solid body from the blood and in the vascular system during life was called a thrombus and defined as an antemortem clot formed in the vessels, the process being termed thrombosis; the conditions are not the same as in clotting outside the body and the make-up of the thrombus is not that of a coagulum. A thrombus is a solidifying body formed during life within a blood channel from fibrin, blood cells, and blood plates in varying proportions. It may be *red* when developed from stagnant blood, *white, laminated* or *mixed* when formed in a current. The thrombus in the first case contains both red and white cells entangled in fibrin,

which is arranged in granules or threads often disposed radially about apparent centers. The *white* consists chiefly of fibrin and white cells and blood plates. Thrombi of blood plates alone do occur, the plates being the result of precipitated globulins or derived from the red cells, and may be the first step in the production of one of the ordinary thrombi. Under the microscope the cellular elements and the fibrin in granules or rays may be readily recognized, and hyaline areas are often found, representing altered plates. The immediate cause of the thrombosis is the interaction between fibrinogen and fibrinoplastin (paraglobulin) under the influence of a ferment and in the presence of a calcium salt. The ferment may come from the white cells, from the erythrocytes or from the vessel wall, and has been supposed to be phosphoric acid or nuclein containing phosphorus.

*Causes of Thrombosis.*—The factors leading to such a thrombosis are three, all pathological and often associated, namely, *changes* in the *vessel wall,* especially in the intima, *slowing* of the *current* and *changes* in the *blood.*

Lesions of the vessels do not cause thrombosis until the endothelial lining is affected. The most common causes are mechanical injury, as torsion and ligation, the formation of atheromatous plates and ulcers, toxins due to bacteria, impaired nutrition and degeneration of the lining cells, phlebitis and arteritis; they all probably release fibrin ferment and increase the tendency of some of the elements of the blood to cling to the vessel wall.

The blood-current may be retarded or stopped by pressure from without, by foreign bodies and parasites in the vessel, by weak heart action, often associated with gravity, or by aneurysmal dilatation with consequent eddies and areas of slow flow and rough surfaces. Emboli always lead to the formation of thrombi where they lodge.

Under the third head, of altered blood, we note the tendency toward coagulation in pregnancy, in chronic nephritis, in rheu-

matism, diphtheria, and typhoid, and in other cases of prolonged high fever, from microörganisms and their toxins, and with increase in the number of blood-plates in some essential anemias. Calcium salts and nuclein favor coagulation; oxalates, oily substances, sodium fluoride and albumose tend to retard it.

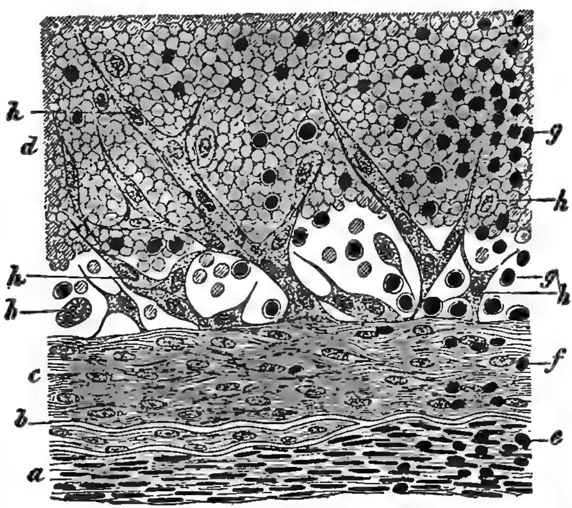
*Varieties.*—Thrombi are called from their

*color,* red, white, gray, or mixed.
*structure,* laminated and stratified;
*time of formation,* primary and secondary, the latter said to be propagated;
*shape, situation, action, infection,* etc.:
obstructing, if vessel occluded;
valve, if current permitted;
parietal, as on wall of aneurysm;
annular, in ring form;
canalized, if blood channels through it;
ball, if detached;
surgical, after litigation of vessels;
cardiac polypi, attached to heart wall;
fibrous, if partly organized;
marasmic, formed in the course of asthenic diseases;
simple or aseptic if free from bacteria;
infected, septic, or putrid if with bacteria;
arterial, venous, portal, capillary, according to vessel involved.

*Further Changes.*—The commonest results in case of simple thrombus are shrinking and drying, alteration of the blood-pigment with change of color in the mass, and final organization. If lime salts are deposited in it we find a phlebolith, arteriolith or, rarely, cardiolith, according to the site of the process. The center of the thrombus, being least supplied with nourishment, may soften and be washed away, permitting the return of the circulation, the softened portion being a reddish-gray syrupy fluid made up of fat, albuminous and pigment

granules which may be too small to cause appreciable embolism. If the thrombus is infected this softening is the usual course and the result is multiple infectious embolism with miliary abscesses wherever they lodge. In the organization of the simple aseptic thrombus the fibrin is pierced by new vessels from the vasa vasorum which carry new connective tissue with them and so gradually replace the fibrin. This new tissue

FIG. 5.




ORGANIZING THROMBUS 3 WEEKS AFTER LIGATURE OF AN ARTERY. (*Ziegler.*)

*a*, media; *b*, elastic layer; *c*, intima, thickened by productive inflammation; *d*, coagulated blood; *e*, cells infiltrating the media; *f*, the same in the intima; *g*, round cells in thrombus and between it and vessel wall; *h*, various forms of new connective tissue cells.

then contracts and at a later date we have only a small fibrous nodule which may be hard to recognize as a former thrombus. Quite commonly a portion of the proximal end of a thrombus is torn off by the blood current, the thrombus always forming up to the nearest collateral branch, and the portion is then carried till it enters a vessel too small for its passage; it comes to rest, plugs the vessel and is termed an embolus.

*Results of Thrombosis.—*

In vessel, organization:
- softening;
- abscess, if infected.

In general circulation:
- according to rapidity of formation;
- nature and size of vessel;
- establishment of collateral circulation;
- force of the current.

In the tissues, if in artery:
- anemia till collateral circulation;
- infarct, red or white;
- death of tissue, dry gangrene.

If in a vein:
- passive hyperemia, stasis;
- hemorrhage;
- edema;
- dropsy;
- moist gangrene.

**Embolism.**—The term is applied to the plugging of a vessel by a foreign body. This may be a piece of a thrombus from a larger artery or vein, coagulated fibrin from a heart valve, fluid fat from a recently fractured bone, air drawn in through the veins, fragments of neoplasms, pigment from disorganized hemoglobin, parasites and microörganisms, hyaline material after extensive burns, dust and mineral matter. The most common are small blood clots, and the seat of arrest is often at the bifurcation of the vessel. If the foreign body comes from the veins or the right side of the heart it is usually caught in the pulmonary circulation, though a *retrograde* embolism as of the hepatic vein, may be caused by convulsive action of the thoracic muscles and the diaphragm, which by extreme increase of intrathoracic pressure drives the venous current in the great veins in a reverse direction. From the left side of the heart an embolus is apt to lodge in the brain, often in

the middle cerebral artery, or go on to the spleen or kidney. Emboli may occur in any artery and doubtless the peripheral are overlooked as their effects are less marked. If the foramen ovale is patent an embolus may be carried directly from the right to the left side of the heart without going through the pulmonary vessels, and pass into the systemic circulation giving a *crossed* or *paradoxic embolism.* After fractures of the large bones of the limbs the fat set free from the injured marrow may lodge in the lung capillaries, causing *fat embolism* of the part and if in vast quantity, asphyxia and death. Air drawn into the veins may also lodge in the pulmonary capillaries, but unless in large amount may not cause any symptoms; when fatal it is because the froth in the right side of the heart gives it nothing to contract on, and hence the circulation stops after irregular cardiac action. Neoplasms are often carried from one organ to another by means of small emboli, as when an ulcerating carcinoma of the stomach opens small radicles of the portal veins, causes malignant thrombus in situ and thence small fragments are borne to the liver, setting up a new carcinoma wherever they lodge. Dust, flour, clay, metal particles and other minutely divided foreign matter may be inhaled and laid away by phagocytes in the bronchial lymph nodes. When one of these softens and breaks the foreign material may cause capillary embolisms passim, leaving the body at last by way of the liver and the intestinal glands.

The *results* of an *embolism* vary with the importance of the part affected. If the vessel is a coronary or cerebral artery death may be immediate, as also after large pulmonary embolism. If small and soft the embolus plugs the vessel completely, if harder, only after thrombus develops about it. The territory supplied becomes anemic with loss of heat and function. This may be relieved by a collateral circulation; if not relieved we may find infarction or necrosis, and if the thrombus is septic, abscesses surely develop.

*Portal embolism* may develop after dysentery, simple or

amebic, carcinoma in any part of the alimentary canal, pylephlebitis, etc., and the usual result is hepatic disease, because the embolus passes from smaller to larger veins until it reaches the portal subdivisions within the liver; as emboli from such sources are usually septic it is common to find hepatic abscess as the result of suppuration throughout the interlobular veins (pylephlebitis).

**Infarction.**—Certain arteries do not anastomose and hence are called "end arteries," as those of the retina, spleen, kidney, heart and brain, and still others have but imperfect and few anastomoses. When such a vessel is plugged by an embolus its cone of distribution becomes anemic and necrotic. The area is called an *infarct,* the process *infarction.* In gross appearance the infarct is cone or pyramid shaped, its apex in the tissue and its base on the surface, which is raised above the general level if recent and slightly depressed if old. Infarcts may be *red* or *white,* and either may be *pyemic.* The white infarcts are formed as described and are of an opaque yellow-white or gray. The red are formed by the entrance of blood into the anemic area, either by reflux through the veins, pressure in the plugged artery being nil beyond the embolus, stasis of this blood and diapedesis; or the diapedesis comes from dilated capillaries along the borders and the cells enter along the slant height of the pyramid, in which case even in the red form the center is usually lighter than the periphery. The formation of red infarcts is chiefly a matter of relative pressures in artery and vein; with pressure at its lowest in the former the tendency is toward red infarcts. If not septic, the necrotic tissue may become organized and replaced by connective tissue, which contracts and dimples the surface, a more or less radiating scar with a certain amount of pigment or of calcareous deposit being all that remains. If the artery plugged is already the seat of disease, or if the embolus is infected with bacteria of less than the highest virulence, the vessel wall may be destroyed and an aneurysm

formed, or necrosis of the tissues about may follow and abscess formation. Infarcts sometimes occur in the lungs when the circulation is very much slowed, and here the infarct may become infected secondarily from some of the bacteria inhaled.

**Hemorrhage.**—Strictly speaking, hemorrhage is the massive exit of blood from a vessel. If blood plasma alone leaves the vessel it is called a *transudate,* and causes edema; if the white cells pass out it is called *emigration* of the leucocytes; if red cells, it is *diapedesis;* in hemorrhage all three are lost. This may be on the surface of a wound, under or upon a mucous or serous membrane, into one of the body cavities or into the tissues. Hemorrhages are called arterial, venous or capillary according to the vessel, mixed or parenchymatous if from all, and are divided into two kinds, namely, by *rhexis,* when the vessel-wall is broken, by *diapedesis,* when it passes through the wall of a capillary or small vein without rupture of the wall. According to their situation and size, they may be called:

*Petechiae,* if under the skin and small as flea-bites; *vibices,* if long and narrow, like strokes of a lash; *ecchymoses,* under the skin, of larger size, with but little destruction of tissue, and after injury; *purpura,* in many small scattered spots under skin and mucous membranes; *suggillation* or *suffusion,* when of large size, infiltrating the tissues; *hematoma,* when large and forming a distinct tumor.

Other names are given according to the cavity into which blood escapes, as hemopericardium, hemothorax, hematomyelia, etc.:

According to the channel by which voided, hematemesis, hemoptysis, hematuria, etc.:

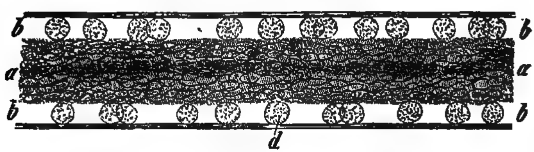
In brain, cord and lung, apoplexy of the part.

Simple outwandering of red or white cells, as seen in passive hyperemia, can not be called a hemorrhage, even though small hemorrhages per diapedesin can not always be distinguished from the former. The physical appearance of a hemorrhage depends upon the vessel from which it comes, whether a vein

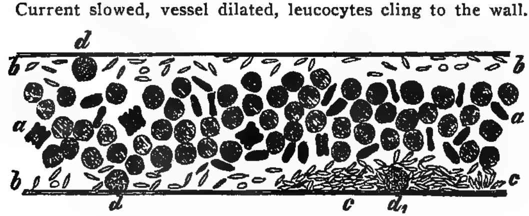
or an artery, but sooner or later in either case the blood extravasated into the tissue interspaces undergoes a regular set of changes. First the red cells are broken up and their coloring matter, altered into brown or black pigment, is left in situ or absorbed. The white cells emigrate in small part or are destroyed like the red, fibrin forms, the clot shrinks, the area becomes walled off by a connective tissue capsule and itself organizes. All this new tissue contracts, lime salts may be deposited, and what remains may be a small fibrous induration, slightly pigmented. Large extravasation from an artery may

Fig. 6.


Normal swiftly flowing blood.




Current slowed, vessel dilated, leucocytes cling to the wall.




Stasis nearly complete. Vessel dilated, axial column breaking up.

Normal and Delayed Blood Stream (*Ziegler.*)

*a*, axial stream; *b*, lateral space, with occasional leucocytes in A, with many leucocytes in B, with blood plates added in C; *c*, collection of blood plates; *d*, *d*, white cells.

remain in connection with the vessel, receiving new blood and pulsating with the arterial throb, and thus forming a false aneurysm.

The *cause* of *rhexis,* break in the vessel wall, may be injury

from without or within, pressure on a wounded place as when a vessel is contused and breaks much later, disease of the vessel wall, removal of support, invasion by tumors and from diseases of adjacent parts. Newly formed vessels and those in tumors are especially liable to break. The blood-pressure may be increased by violent heart action, obstacle to the venous flow, mental emotion, thoracic spasm as in coughing, asphyxia in the new-born and from other causes.

Diapedesis occurs through the bodies of the endothelial cells of capillaries and small veins or through the intervals between them; the idea of stomata has been generally abandoned. It occurs where the pressure is much increased or the vessel walls are abnormally permeable, from bacterial toxins, or prolonged heat, and is seen specially in certain cachexias. The tendency to loss of blood, either spontaneous or disproportionately large after injury, may be congenital, often hereditary, and is called *hemophilia*. A similar tendency may be acquired in scurvy, certain contagious diseases with high temperature, as typhus, malignant endocarditis, yellow fever, and in certain essential anemias, where the blood is disordered and the vessel walls suffer in their nutrition. The influence of the nervous system is strong in producing certain hemorrhages, as in hysteria with stigmata, vicarious menstruation with or without genital anomalies, and disease of the brain, especially the crura, with bleeding in lungs or parts of the alimentary canal.

*Effects.*—Death may follow from the amount of blood lost (1-20 of the total volume). The patient may faint from cerebral anemia and recover with a slight fever. The heart action becomes slow and feeble, thus favoring clotting and control of the bleeding; the fluid lost is then made up by absorption from the tissues, stoppage of excretions, and ingested fluids. Repeated small hemorrhages may be fatal; single ones sometimes appear of benefit to the organism.

**Lymphorrhagia, Edema, Dropsy.** Loss of the contents of a lymph vessel is called lymphorrhagia. It is soon checked

by counterpressure of the tissues unless on the surface of a wound or a serous cavity. Thus injury to the thoracic duct, either direct or secondary to other lesions, may cause extravasation of lymph into the pleura or the abdomen; and the presence of the tropical parasite Bilharzia hematobia in the lymph channels may cause escape of lymph into the bladder and hence chyluria, or milky urine.

From its frequency a far more important interference with the lymph stream is seen in the condition known as edema. White cells and the fluid part of the blood normally leave the capillaries for nutrition and repair of tissues. This fluid is the tissue lymph and is not identical with plasma, as is shown by the fact that it is often richer in salts and sugar, poorer in albumin, of lower specific gravity and does not coagulate spontaneously. Such a fluid is called a *transudate,* to distinguish it from the fluid of ascites and *inflammatory exudates.* When such a process is excessive in the superficial tissues it is called *edema* and is most marked in lax and dependent parts, as the scrotum and the ankles; when general it is called *anasarca.* If the fluid accumulates in cavities it constitutes hydro-pericardium, hydrops articuli, hydrops abdominis or ascites or "dropsy." The belief that the serous cavities are expanded lymph spaces has been disproved by embryological study, and great as the analogy may be, collections of fluid in them are not the same as edema in the tissue.

The cause of edema is usually hindrance to the venous return, *e. g.,* in the abdomen from atrophic hepatic cirrhosis and compression of the portal vein by newly formed connective tissue in the liver, or from cardiac valvular disease. The fluid is rich in albumin and of high specific gravity. It may hold flocculi of fibrin in suspension, may coagulate spontaneously, and is often colored by the addition of blood or bile pigment.

Six factors enter into the production of edema, usually more than one acting at a time, viz.—positive pressure in the vessels (in proportion as it rises), permeability of the vessel wall, osmosis from excess of salts outside the vessel as seen in the

action of a saline laxative, selective action of the endothelium, variations in the blood plasma, and obstructed onflow in the lymph channels.

We distinguish several varieties, viz.—(1) edema of active hyperemia; usually slight, though as a stage of inflammation it may reach a high degree, as in the lung.

(2) Edema of passive hyperemia; the cause an obstacle to venous return, the classic example cirrhosis hepatis; also from heart disease, vesicular emphysema and obliteration of lung capillaries, or pressure from a gravid uterus with phlegmasia alba dolens; in all, a simple leaking from distended weakened vessels.

(3) Edema from obstruction to lymph channels; as pressure on the thoracic duct, parasites in the channels; often lasts a long time without symptoms because of free anastomosis.

(4) Edema of cachexia; the blood being altered, nutrition of vessels impaired, combined effect is transudation.

(5) Toxic edema, from action of microörganisms and their products on vessels and blood.

(6) Inflammatory edema; here the fluid is called an *exudate,* is rich in albumin and cells, and coagulable.

(7) Neurotic edema; as in the vesicular skin eruptions, dropsy with neuritis and diseases of the cord, a trophoneurosis in most cases.

Whatever the cause, edematous parts are swollen, pit on pressure, if superficial have a lowered temperature, function at first less and then lost, fluid in the interstices and then cells and fibers of the part swollen, area disposed to fatty degeneration and necrosis. (See Coagulation necrosis.) In the organs, as the lung, the part is swollen, dense and pale, its histological elements are pushed apart, and on coagulating the fluid by boiling water it is found to be not only in the alveoli but also in the tissue spaces themselves. Such a tissue when cut exudes a large amount of usually clear fluid. If there is a prominent mucous element, as in disease of the thryoid, it is called *myxedema.*

# CHAPTER IV.

## DISORDERS OF METABOLISM; CONSTITUTIONAL.

*Metabolism* is the collective term given to the entire series of physiological processes by which the organism acquires nutriment, prepares it for the nutrition and repair of its parts and rejects such elements as are not available. Obviously, then, metabolism, implying the activity of so many organs and the integrity of so many separate processes, may suffer such alterations at any one of the numerous stages as to become pathological. The abnormality may be one of function or of structure, usually the former precedes the latter and both coëxist by the time they become the object of study.

Metabolism disorders of the organism as a whole may occur along two lines, either in the nature of the pabalum supplied or in the use made of it. The pabulum may vary in either amount or quality, but it will be convenient to discuss it as either excess or defect.

If food and drink are taken in larger amounts and more frequently than is required for the bodily needs, the excess either passes out of the intestines undigested (its previous putrefaction may have serious consequences), or it causes an overfulness of the blood-vessels (plethora) or general increase of the body fat (obesity). Such persons are often characterized by ruddy complexion, prominent vessels and eye-balls, great activity, muscular or mental, copious defecation, high-colored urine and tendencies toward active congestion in various organs. On the other hand, when nutriment is supplied in too small quantity or poor quality, or what amounts to the same thing, the digestive powers cannot make use of good food,

the bodily weight diminishes, its heat likewise and all its energies. Collections of fat and glycogen are consumed, except in the case of fatty new growths; fat is lost from heart, kidney and nervous tissue last. Respiration and pulse-beat become slow and feeble, the fluid part of the blood is lessened and its cells also, though they show a relative increase; secretions and excretions are less in amount and altered in quality; mental torpor alternates with delirium, and death occurs from exhaustion (*inanition*) or from the products of altered gland action. When similar conditions develop in the course of a definite disease it is termed a *cachexia,* and while all cachexias have starvation in common, they vary according to the effect of the concurrent disease. Thus we speak of *marasmus* in the newborn and the aged, *anemic, malarial, cancerous, suprarenal* and other cachexias. Starvation is understood to refer to food supply, but lack of oxygen in all its forms is also a starvation and manifests itself as air-hunger, dyspnea and cyanosis; local starvation ends in atrophy or necrosis.

*Misuse of Pabulum.*—Food taken, though of good quality, may be wrongly used, either in the anabolic or the katabolic series of changes; or there may be excessive tisue waste apart from the amount of food ingested. In certain cases the origin of the trouble may be sought in the alimentary canal or tributary glands, in others the emunctories are at fault and retain matters which are noxious in their effects.

Three chief types of these intoxications may be recognized:

1. Some important function may be impaired, with or without tissue changes, especially in the glands which prepare incomplete metabolic products for further elaboration. As examples may be cited Addison's disease, acute yellow atrophy of the liver, myxedema and pancreatic diabetes.

2. Intermediate and toxic products of metabolism may enter the general circulation without any localized lesion, as in diabetes, gout, oxaluria.

3. Products of retrograde metabolism which should be ex-

creted are retained in the circulation or the tissues, as carbonic acid gas in dyspnea and carbon monoxide poisoning, various excreta in uremia. At times the formation of such products may exceed the ability to excrete them by the emunctories and this may be due to increased production or decreased elimination, with steady accumulation in either case, as in carcinomatous and diabetic coma, acetonemia, cystinuria.

*Acid Intoxication.*—From albuminous food both sulphur and phosphorus may furnish corresponding acids, and lactic, sarcolactic, oxybutyric and other acids may be developed. The excess in part is neutralized by ammonium and fixed alkalies, in part split into other bodies, as acetone and diacetic acid; imperfect oxygenation usually coexists. The constitutional effects are disturbance of pulse and respiration, marked dyspnea, stupor and coma, as seen in diabetes; to a slighter degree such symptoms occur in many fevers, carcinoma, acute yellow atrophy of the liver, phosphorus poisoning.

*Albumosuria.*—Where there is rapid tissue destruction albumoses or peptone may form and appear in the urine; a certain excess of leucocytes usually accompanies the symptom, but the details of the condition are still obscure.

*Intestinal putrefaction* is a common result of imperfect use of food and leads to many of the well-known self-intoxications. The process is extremely complicated and more than one type may be recognized. Fermentation may occur in the stomach and causes the dissolution of carbohydrates; it may be of the acetic, butyric, lactic, or alcoholic form. Putrefaction occurs in the intestine and concerns proteids; its products are chiefly cystin and methyl-mercaptan, or amido-acids, or substances of the aromatic series, as acetone, cresol, indol, skatol and tyrosin. Ptomains are also present and may account for many of the symptoms. If food decays outside the body and is then eaten, it poisons by the ptomains in it; similar effects follow putrefaction in the gut. Many of the alkaloidal bodies of albuminous decay resemble strong vegetable alkaloids, strychnine, morphine,

etc., and in the usual cases the patient may exhibit digestive and nervous symptoms like those caused by repeated small doses of such drugs. If the poisons are too irritating, an attack of diarrhea may result and relieve for a time. In more severe degrees, especially when the kidneys do not eliminate absorbed poisons, *copremia* results, with indican and ethereal sulphates in the urine, cold surface, cramps, convulsions, perhaps death in coma. The extract of 2.5 gm. of putrid feces is fatal to an animal weighing one kilo. In the chronic forms of slight degree, often with crises and exacerbations, the skin and mucous membranes are subject to inflammations of various kinds, melancholia and hypochondriasis often follow, and in the infant, rickets.

*Icterus.*—The bile contains fats, biliary acids and salts, soaps and cholesterin, and coloring matters; these latter are bilihumin, biliprasin, bilifuscin, biliverdin, bilirubin.

These are all derivatives of the last, bilirubin, which resembles hematoidin, and in poisonous effects from bile resorption it is the coloring matters which are the chief element; bile deprived of the coloring matter by filtration through charcoal becomes one-third as toxic as entire bile. The daily amount of bile varies from 800 to 1,200 cc. for the adult, enough to kill three men of average weight if injected into the veins, or enough in 8 hours, if absorbed, to cause physiological suicide. The great safeguard against poisons from the intestine is the liver, which destroys them and excretes them into the duodenum again; against poisons circulating in the blood the kidneys perform a similar office of elimination. Normally the acid contents of the stomach on reaching the intestine cause a precipitation of the bilirubin in the form of insoluble granules; if from interference with its excretion a stasis of bile occurs in the liver it may gain entrance to radicles of veins or lymphatics and thus enter the general circulation. Were it not that part is eliminated rapidly by the kidneys and the excess deposited in the tissues of the connective type, fatal

poisoning in this condition would be more common. Cholemia may be considered also as an acholia rather than a hypercholia. Some urea is formed in the liver from ammonium carbamide, but with impaired hepatic function this is not formed and also certain poisons from the alimentary tract may slip through into the general circulation (arsenic, glycocol, amido acids). Recent opinion tends to consider the bile salts more poisonous than bile pigments.

*Excessive Catabolism.*—Apart from tissue waste in starvation, there may be extreme destruction of various cells in fever of any sort, new growths, especially carcinoma, Basedow's disease, phosphorus poisoning, and many other conditions. The cause of the great waste is partly the degeneration following high temperature, partly the accompanying disorders of cell nutrition, and at times the production of some toxic substance peculiar to the special disease. Such hypercatabolism is therefore a feature of many clinical pictures rather than a disease in itself.

*Disordered Secretion and Excretion.*—Here two groups may be recognized, with many transitions and combinations; cases where something of value to the organism is lost by way of the emunctories, and cases where excreta are retained. One of the most important cases of the former is *albuminuria,* the excretion of serum albumin and serum globulin by the kidney in consequence of damage to the glomerular and tubal epithelium of the kidney; this regularly accompanies various forms of nephritis and will be treated in that relation. If blood as such occurs in the urine it is called *hematuria,* if the blood pigment, *hemoglobinuria;* the former occurs most often when the urinary organs and passages are diseased, the latter when the circulating blood is affected and its red cells destroyed, as in malaria. *Dextrose* or *glucose* lost by the urine is the distinguishing symptom in *diabetes,* though it occurs as a transient symptom in some nervous diseases or even after large use of sugar and carbohydrates in the diet. Normally, the

liver arrests sugar coming from the alimentary canal; if imperfect function allows some to pass we have an alimentary glycosuria or more persistent forms. Extirpation of the pancreas causes diabetes, for the regulative function of the gland is removed and more sugar reaches, and passes, the liver. In the blood sugar is a protoplasmic poison, causing increased catabolism and nitrogenous elimination.

A good example of retained excreta is furnished by *uremia*. The daily amount of urea excreted in health varies from 30 to 40 grams, and its retention was supposed to cause the symptoms grouped under the name of uremia. The urine contains seven or eight toxic substances which have been recognized, among them one which causes lower temperature, one causing myosis, one causing coma, and also potassium, a tissue poison, urea and other organic poisons. No one of these will produce experimentally the features of human clinical uremia and it is probable that the condition is due to imperfect excretion of urine as a totality rather than a single ingredient, which may account for the many forms of uremia as one or another element prevails. In pregnancy the urine becomes less toxic, the serum more so, hence puerperal eclampsia may be a retention-toxemia. But it has been supposed that the fetus may elaborate a substance toxic for the mother, for the case at times differs from other uremias.

In *Addison's disease* the intoxication may be due to the absence of the regulating influence of the adrenals on the neurin in the body, as the thryoid may be supposed to affect the metabolism of mucin and the pancreas that of sugar; but severe lesions of the adrenals may be found with no history of suprarenal melasma, and the intoxication may exist without characteristic changes in these organs.

Connected with the thyroid gland four conditions are recognized, *cretinism, myxedema, cachexia strumipriva* and *Basedow's disease*; in the first three the function of the gland is imperfect or lost, in the last the picture is rather that of ex-

treme activity. Thyroid gland supplied in the first three usually relieves the symptoms, in the last it aggravates them, and it may produce similar manifestations in the healthy. Three explanations are offered for these conditions: Either the gland produces a toxic substance from morbid function, or the normal product is excessive, or the gastro-intestinal tract prepares a toxic substance from mucin because of impaired control by the thyroid body. (See p. 420.)

*Oxaluria* and *phosphaturia* are conditions of the urine when it holds an excess of oxalic acid salts (calcium) or of phosphates. Both occur as an expression of defective metabolism and tissue waste, in dyspepsia with imperfect carbohydrate digestion and retention of intermediate products, nervous functional disorders, and bone diseases.

*Acetone* and *diacetic acid* in the blood and urine are often found in the later stages of diabetes and hence are of grave clinical significance.

*Uric acid* retained in the system is closely connected with gout.

*Hydrothionemia* is occasionally seen, due to the presence of sulphuretted hydrogen in the blood; in such cases the gas can be recovered from both urine and feces.

## Appendix to Chapter IV.

*Fever.*—Clinically the essential symptom in fever is elevated bodily temperature, but with that the heart action is increased in force, frequency, or both, the process of respiration is involved and the urine shows the effects of increased tissue waste. When the normal balance between heat production and heat dissipation is lost we may have lowered or elevated body temperature as the result; if high, the temperature is a *fever temperature.* The normal temperature of the body is stated as 98.8° F. (37.2° C.), with daily variations of part of a degree less in the early morning and as much higher in the

evening, and in fevers these variations are often reproduced on a higher level. *Moderate fever* runs between 101° F. and 103° F.; any temperature over 105.5° F. is called *hyperpyrexia;* such very high temperatures are seen in exanthemata, pyemia, sunstroke, and occasionally in hysteria. The nature of fever is still obscure in many points. The source of the high temperature may be chemical rearrangements of the ultimate elements of body cells and consequent liberation of energy in the form of heat. Probably these chemical reactions, especially of the catabolic series, have their reaction-velocity accelerated under the influence of disordered innervation. The *etiology of fever* includes insolation, nervous disorders, infection by various microörganisms and the effect of their ferments and toxins. Its *results* are emaciation, degeneration of glandular and muscular cells, loss of function in any structure, and death from the tissue changes or the retention of excreta; recovery is possible as long as the violence and extent of such alterations are relatively limited.

Many fevers present well-marked stages in their development:

*Initial stage,* the temperature rising to the height characteristic of the special disease, usually in a few hours; if sudden, accompanied by a chill, which is an expression of disordered innervation, an explosion of motor energy setting the muscles, voluntary and involuntary, into irregular, convulsive activity. The chill begins usually with vaso-constrictor spasm of peripheral arteries which causes subjective coldness.

*Stage of Acme, or Fastigium.*—Temperatures fairly stationary about a daily average, with slight morning fall and equal evening rise.

*Stage of Defervescence.*—Fever temperatures returning to the normal rapidly, with general improvement, often accompanied by sweating, said to end by *crisis;* where defervescence is protracted over days, by *lysis.*

Typical typhoid fever shows these stages very clearly, the curve for the four weeks being roughly described as, "first week staircase, second week stationary, third week remittent, fourth week intermittent."

The cyclical nature of many fevers is perhaps to be referred to the death of the causing organisms after they have exhausted the substances in blood and tissue which are available for their nutrition, or after their products reach a percentage beyond which they inhibit the growth of the producing organisms, or after the body cells have produced a substance which is fatal to the organisms. The subject is entirely a matter of supposition, but the self-limited nature of many fevers is one of their clearest characteristics. (See Immunity, p. 238.)

# CHAPTER V.

## DISORDERS OF METABOLISM; LOCAL.

DISORDERS of metabolism may be *local,* and then we find that the disorder is either *quantitative* or *qualitative.* Local metabolism disordered quantitatively may err either in excess or defect; as excess we have hypertrophy, hyperplasia, and metaplasia; as defects we have agenesia, aplasia, hypoplasia and atrophy.

*Hypertrophy.*—The term hypertrophy is applied to the increase of a part with increased function, without departure from normal structure or chemical composition, and it may be physiological or pathological. The significance of the term is often relative, for a kidney weighing six ounces is normal if found in an adult but hypertrophied in a child, and it may be difficult to define the limit beyond which the size and weight of a part justify the name. In a hypertrophied tissue the various elements are supposed to be larger than normal (uterus at term), without numerical increase, and hyperplasia is reserved for the latter condition. The distinction is not of great value in the physiological hypertrophies but perhaps has significance in the pathological; thus the more numerous bile ducts in atrophic cirrhosis are strictly a hyperplasia.

Hypertrophy may be congenital, manifested as a giant growth of the whole body or a part of it, or it may be more localized to one form of tissue, as skin, hair and nails; or such extra growth may develop in after life without apparent cause, as in the case

of cutaneous horns. Other cases of hypertrophy may be traced to heightened functional activity, as in the muscles of the athlete, the waste of the muscle cells being more than made up by extra nutrition and this excess manifesting itself as increased size. Certain forms of hypertrophy are called *compensatory* and certain others might be called *vicarious*, an example of the first being furnished by one of paired organs which takes up the function of the other and with the greater activity increases in size, and a good instance of the second is found in the tactile development of the blind.

*Pathological hypertrophy* is usually due to irritation and its sequel, inflammation, or it may be compensatory, as in the cardiac ventricles when they have to overcome increased resistance due to pulmonary and valvular changes. A simple case of the effect of irritation is seen when intermittent pressure and friction increase the thickness of the epidermis; certain inflammatory discharges will also cause local hypertrophy of the integument, as warts and condylomata. When larger areas of integument are involved, as in elephantiasis, the part may reach many times its normal size. The spleen and the lymph nodes enlarge in some forms of constitutional disease, perhaps in part from overwork, and distal portions of the skeleton may hypertrophy, as in the disease called acromegaly, with or without alterations in the hypophysis cerebri. At times the response to irritation is hyperplasia, numerical increase, though the new formations are not larger than normal, as seen in the new bile ducts of cirrhosis.

*Metaplasia* is the name given to the alteration of a tissue into one of another variety and is a term of very limited application, confined almost wholly within the borders of the connective tissue group. Thus hyaline cartilage may become fibrous, and mucous tissue may become adipose, and such changes are seen in both physiological and pathological processes, but epithelium never becomes fibrous connective tissue or vice versa, though columnar epithelium may become squam-

ous. The altered tissue most often does not persist and the metaplasia may be considered as a stage of a degenerative process; in many cases it belongs in the qualitative disorders of metabolism.

*Anaplasia* is a term applied to the cells in tumors, especially of malignant forms. These cells tend to lose all their acquired specialized characters and return to an undifferentiated type like the cells of the early embryo. This constitutes a marked feature of new growths and distinguishes them from inflammatory hyperplasias. Connected with their rapid multiplication the tumor cells have large nuclei, rich in chromatin, and present many mitotic figures. They are large and apparently functionless. All these characters are included in the word anaplasia. v. p. 152.

*Heteroplasia* is the development within a formed tissue of a new tissue foreign to that locality, though perhaps normal elsewhere, and while the effect is sometimes increase of the size of the part, yet it belongs strictly in the qualitative series.

**Metabolic defects** may be congenital and are illustrated by all dwarfed and arrested development. In some cases an entire organ may be absent, one kidney or part of one cerebral hemisphere, and to this the name *aplasia* or *agenesia* is given. Where a part has started to develop but has not attained a development proportional to other parts it is termed *hypoplasia,* and a good instance is furnished by hypoplasia of the aorta and of the lower half of the body in consequence. This condition is met with in certain cerebral hemorrhages in early life and points to general arterial hypoplasia as the explanation.

When a part has once acquired the proportions normal for the time of life when it is studied, and then loses in size, and usually also in function, it is said to be atrophied and the process is called *atrophy*. Many cases of so-called atrophy are strictly hypoplasia, as in chlorosis associated with undeveloped genitals, and the dwarfed mind and body of cretinism. Although atrophy is often observed with various forms of degeneration

and may lead directly to one or the other of them, it is to be distinguished from degeneration by the fact that the latter involves cellular death in the part; atrophy merely implies diminution in size. Atrophy often follows closely upon hypertrophy, the size which an organ may reach being apparently limited in any case, as is true of the body as a whole.

Certain forms of atrophy are normal in certain life periods, for the thymus gland diminishes at about the tenth year, and the genital organs undergo atrophy with the decline of the sexual function. In a sense the atrophy of muscles confined in splints, and of the cerebral cortex in old age are normal from this point of view. Lack of use or diminished use, with consequent lessened blood supply, covers these cases and also the atrophy which follows nervous lesions. Atrophy again follows mechanical pressure, constriction from adhesions, and diminution of the blood supply from any cause. Certain poisons have an atrophic effect upon certain organs. All the varieties of simple atrophy may be grouped under one of two causes, with associated lessening of function, either imperfect blood supply or imperfect use of the blood supplied.

Atrophy may involve the whole of an organ or only a part of it; in the latter case it is called *asymmetric;* the effect of the latter form it to distort the part unless the defect is made up by another tissue. Thus in atrophy of the cardiac muscle either fat or new connective tissue may replace the lost muscular elements, and in osteoporosis of bone the marrow increases in proportion as the bone substance is lost. Fatty, pigmentary and connective tissue changes are often found in connection with atrophy, but in the majority of instances are associated with degeneration and belong in a later paragraph.

The physical appearance of an atrophied part varies; it is usually smaller in size, it may be variously dimpled and distorted, the capsule if present is thick and opaque, connective tissue replacement makes the organ hard, dense and tough on section, fatty replacement makes it more yielding, the anemia

may give it a lighter color than normal, and pigment, as in brown atrophy of the heart, may darken it. The various steps in the process are, loss of fluid, hence dryness and density, decrease in size and number of cells, vacuolation of cell bodies, wasting of nuclei, accumulation of pigment, waste of high-function cells first, loss of striation in muscle, occlusion and disappearance of vessels, relative or actual fibrous increase, replacement by fat, shrinkage and cicatrization.

**Local Disorders of Metabolism; Qualitative.**—These may vary in two directions, including cases where some substance is added to a tissue, instances of matter out of place and comprising all the varieties of infiltration, and those cases where there is *tissue defect,* including the degenerations.

**Infiltrations** may be deposits of *normal materials* or of *pathological products,* and among the former the material may be either *inorganic* or *organic.*

Certain trades are carried on in circumstances favorable to the ingestion of foreign bodies in a state of fine subdivision, and the favorite seat of deposit in the body is the lung. Probably the dust or other matter is deposited on some part of the bronchial mucous membrane, absorbed by phagocytes and laid away in the tissue framework of the organ or in the lymph node corresponding to the site of deposit. In this way large portions of the lung are colored black by coal dust, a condition known as *anthracosis* and met with in the lungs and bronchial nodes of every dweller in cities and worker in coal. Should the amount of matter thus introduced become excessive, beyond the ability of the tissue to suffer its presence, a peculiar form of pneumonia is apt to develop, known as *anthracotic* or *miner's pneumonia.* Should a lymph node which is loaded with the foreign pigment soften and its contents enter the general circulation, the pigment may be met with in any part which eliminates or passively receives it, as in the liver, bile, and alimentary mucous membrane. Similar conditions occur from working in stone dust, steel-sharpening works, etc., producing

*siderosis, knife grinder's phthisis, chalicosis,* and *lithosis.* Organic dust may be inhaled from working with feathers, hair, shoddy, or wool, and leads to lung affections sooner than in the former case. Workers in brass, zinc, arsenic, phosphorus and mercury suffer from constitutional symptoms peculiar to the metal used, but the discussion of this form belong in the chronic poisonings. Part II., p. 395.

*Calcification.*—The inorganic material does not always come from without; often it is manufactured in the body. Several forms occur. Deposit of lime salt is called *calcification;* this is a normal process in the cartilages with advancing age, seen especially in ribs and larynx, and is an effort at repair and protection where a foreign body is shut off by incrustation or infarcts become calcareous. Other cases are the deposits of uric acid salts, the formation of calculi, "sand" in certain tumors and various concretions.

Though the term calcification refers to salts of lime they are not the only ones found in the tissues; beside calcium carbonate and phosphate, oxalates are often present and the corresponding magnesium compounds. If these salts are in large amount the tissue may be solid with them and is then said to be *petrified,* as is sometimes the case with a fetus in extrauterine pregnancy, the product being called a *lithopedion.* Two forms of calcification are found, one where the mineral matter is deposited in the tissues and another where it gathers round a nucleus in some body cavity; the latter are spoken of as *concretions* and often have various pigments and other elements included in them. Part II., p. 543.

In the tissues the earthy salts are deposited in parts which are either dead or dying; even when as one of the regular changes of advancing age such deposit occurs in the arteries and elsewhere, a hyaline change in the basement substance and an atrophy of the elastic fibers have preceded it. The nutrition of the part involved is always imperfect, as is seen also in some tumors, like uterine fibromyomata, which often bear large

amounts of earthy material scattered through them. Such calcification is not bone formation and must be carefully distinguished from it; the process is passive, the structure of bone is not reproduced and it occurs in a part whose nutrition is below normal. Usually the salts lie in the fibrous framework of the tissue, between the cells, but the latter may also be the seat of the deposit. In either case under the microscope we observe very fine granules in the parts mentioned, highly refractive, dark with direct illumination, which are insoluble in ether but dissolve in hydrochloric acid with the liberation of carbonic acid gas; such bodies take hematoxylin strongly. If the cells are involved the grains occur in the protoplasm and in time hide the nucleus. Such changes occur commonly about foreign bodies, and always accompany trichinæ in the muscles. Other cases are in the apex of the lung, about foci of tubercular infection, in tendons, forming "exercise bones," in ganglion cells and vascular walls in old age and in the kidney after chronic mercury poisoning. A *metastasis* is spoken of when bone is being destroyed in quantity and the lime salts are laid down in distant parts. The chemistry of the process is probably a change of the soluble lactate and glycerophosphate of lime into the insoluble carbonate and phosphate and their precipitation from the blood in parts whose nutrition is impaired, because the presence of free carbonic acid is lessened in such parts.

*Concretions* are formed in some cavity or canal of the body about some other substance which acts as a nucleus, it may be a bit of dead tissue, thickened mucus, or a small foreign body. The chief concretions are the gall-stones and the urinary calculi, others form in the prostate about amyloid bodies, in the pancreatic and salivary ducts, in the appendix and elsewhere. The conditions favoring such formation are an abnormal composition of some excretion, chemical decomposition, the presence of a solid nucleus and something to bind together the various layers of deposit. Thus, as in stone in the bladder,

thickened mucus surrounds the nucleus, earthy salts are deposited in this, again a layer of mucus and a layer of mineral matter, and so on as long as the calculus remains. Gall-stones may contain also, or chiefly, cholesterin with biliary acids and pigment, and are specially liable to form on account of the high percentage of solid matter in the bile (14 per cent.) and the narrowness of the biliary passages.

*Urate Deposits.*—Sodium quadriurate is soluble in the blood plasma and may circulate as a waste product on its way to the kidney, but in certain constitutional conditions it is converted into the insoluble biurate and is then deposited in portions of the body which are normally of relatively low temperature, as the external ear, the small joints of the hands and feet, ligaments, tendons, etc. Such *tophi* under the skin may break through and discharge a thick whitish semi-fluid made up of mineral salts and a little plasma. In the new-born child, during the first week of life, precipitated sodium urates occur in quantity in the renal tubules and often appear in the pyramids as converging yellowish white lines which meet in the papillæ. Such *urate infarctions* are supposed to prove that a child has been born alive and are so far trustworthy that their presence justifies the belief although their absence is not a proof of still-birth.

*Stones* often form in the renal pelvis from calcium oxalate or urates and either remain there and increase or pass down to the bladder and form the nucleus for phosphatic calculi. Wherever concretions occur they may lie quietly for a long time without apparent damage to the container, or by irritation of the part lead to ulceration and perforation.

The sand in the pineal body, choroid plexus and certain tumors, as psammoma may also be mentioned here.

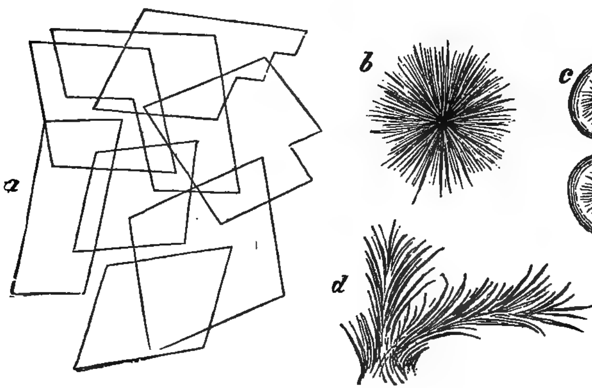
*Fatty Infiltration.*—The essence of an infiltration is the passive accumulation of the infiltrate in the tissue, being usually brought there from a distance and consisting of normal material or of pathological products. If normally present in the part

then the infiltration consists of an excess. The proper cells of the part are normal or suffer passively from the pressure of the infiltrate and consequent interference with function. Fat in and among the cells may be an *infiltration,* when more or less normally present in the part, or an *invasion* when not normally found there. An example of the former would be the fatty liver, and of the latter, fat between the muscle fibers of the heart. That the process is in great part a mechanical overloading and not the result of local cell destruction is proved by the persistence of the protoplasm and nucleus of the cell even when a globule of fat has pushed them far aside; if the fat is removed the cell may recover perfectly. Even when this reaches a high degree, as in the liver, the fat may be dissolved out of the cell by ether and a normally staining nucleus found. Beyond a certain grade, however, the cell contents must suffer atrophy from the pressure. In fatty degeneration the picture is a very different one. There the protoplasm is dying, it contains many fine droplets of fat, and its staining power is nearly or entirely lost.

Fatty infiltration may be the expression of excessive food, fatty and other, or of inability to use a smaller amount of nutriment, or of accumulation of fat in the circulation from destruction of tissue, nervous and osseous, elsewhere. The first is seen in obesity of all grades, the food taken in beyond the bodily needs being laid away in the tissues in the form of fat, and certain kinds of food and drink and an apparent bodily tendency to fat formation, aided by deficient oxygen, are often the factors. Alcoholic patients, beer drinkers especially, often have enormous fat accumulations in the abdominal organs and walls. In such cases the fat appears first in normal situations, under the skin, about the mammary glands, in omentum and mesentery, and in the liver; afterward there is hardly a tissue which may not be invaded. Often but one organ is involved, when the case is one of inability to use the fat introduced, namely the liver, and this may be larger and heavier than

normal from the fat when the general picture is one of extreme emaciation, as in tuberculosis and carcinoma. The explanation is in part that the liver cells can not make use of the fat brought from the alimentary canal by the portal radicles, and partly an actual increase in total amount because these patients for months take nothing but very fatty food, eggs, milk and ol. morrhuæ. In such a liver the fat is found first at the periphery of each acinus, in later stages all through it, and if there is doubt as to its nature the absence of fatty degeneration

FIG. 7.




CHOLESTERIN PLATES, MARGARIN NEEDLES. (*Ziegler.*)

*a*, cholesterin plates; *b-d*, groups of free margarin needles; *c*, the same in fat cells.

elsewhere will show that it is a high grade of *infiltration;* the same degree of fatty *degeneration* in the liver would necessitate a similar degree in other parenchymatous organs. Chlorosis and diabetes, nerve lesions with destruction of myelin, bone lesions with injury to marrow, and certain ages as puberty and senility present other instances, the last two being closely dependent upon disordered blood formation. Another form occurs as replacement for dwindling tissues, as in atrophy of the kidney and increase of its fatty capsule. Where fat accu-

mulation has reached a marked grade small stars of margarin crystals and rhombic tables of cholesterin are found microscopically. In the gross a fatty organ is usually large, marbled and mottled if the fat is irregularly placed, yellow unless congested, less dense but heavier than normal.

*Glycogen.*—Infiltration of the tissues with glycogen, where not normally present, or in excess in proper sites, is purely an infiltration; conversion of cell proteid into this carbohydrate has never been observed. Liver, muscle, cartilage, embryonic and placental tissues normally contain glycogen. If found there in great excess, or in other tissues where normally absent, it appears as glistening, homogeneous granules within the cells, or as balls, often concentrically marked, of more or less regular shape, in various lumina or free in the blood. The amyloid bodies found in the prostate glandules are similar bodies. Such granules are common in the blood of certain anemias and of diabetes, and in tumors formed in parts which in the embryo are rich in glycogen, as chondroma, periosteal sarcoma, myoma. On applying iodin the granule becomes brownish red, on heating or adding saliva the color is lost; amyloid keeps its brown color in the latter conditions and becomes blue on adding sulphuric acid. Glycogen derived from liver, kidney, muscle and leucocytes (and pus) is soluble in water; that from epithelium and cartilage less so. It is insoluble in alcohol, convertible into sugar (maltose) by dilute acids and ferment, and when pure is an amorphous white powder. It resembles both starch and dextrin. In certain tissues it is not found pathologically, as in the infectious granulomata, and most tumors of the histoid group.

*Edematous Infiltration.*— Usually when there is venous stasis or other cause which fills a part with edematous fiuid, the cells escape for a time, merely pushed apart by the infiltrate or compressed by it; but after a time the cell body takes up the fluid, becomes distended even to bursting, and fatty or other degeneration follows. Many skin disease associated with the produc-

tion of vesicles and blebs exhibit this phenomenon, as also superficial burns, certain inflammations and beginning cloudy swelling. It is noted also in congenital edema and syphilis. It can be seen in granulating wounds treated by water-bath and in epithelia kept in the moist state.

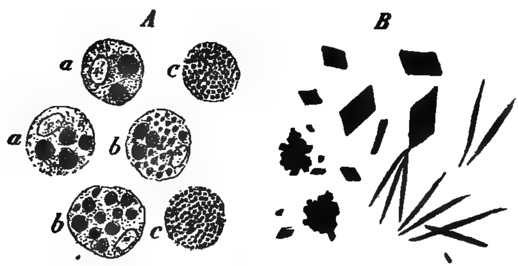
*Cholesterin.*—Fatty detritus from decomposing tissue and exudate, as in sebaceous cysts, often contains thin plates of cholesterin. They are four-sided with reëntrant angles at one corner or along an edge, and may be visible as little shining specks. Cholesterin is found normally in the bile, held in solution by soaps and bile acids. It is soluble in benzol, chloroform and ether, turns red with sulphuric acid and appears in both fatty infiltration and degeneration, especially the latter.

*Pigment.*—In the vast majority of cases the deposit of pigment in the tissues is a passive process, a true infiltration, and its origin may be outside the body or internal. Dust inhalation has been mentioned; tattooing is a common form of introduced pigment, and it has been claimed that workers in brass absorb metal particles through skin and hair-follicles. A better instance of foreign pigment is the condition called *argyria*, due to long use of silver as a drug; the pigment is found in the stroma of many tissues as fine brownish grains, probably silver albuminate colored by light. The skin, the alimentary mucous membrane, the choroid plexus, and the medullary portion of the kidney are the favorite sites of deposit; epithelia usually are free.

Of the pigments found in the body, normally or pathologically, some are the product of cell activity and perhaps formed from albumin (this is denied by many observers), and often contain nitrogen and sulphur, some are formed from the blood by the cells, and others come from destruction of the red cells, either as extravasation and hemorrhage or while still circulating. The most important pigments are hemoglobin, methemoglobin, hemoisiderin, hematoidin, hematin, hemin, hemofucsin, melanin, lipochrome, and of ochronosis, malaria, and the bile.

Normal sites for pigment are the rete Malpighi of the skin, the retina, fatty tissue, corpora lutea, the pia and choroid, ganglion cells, etc., and in most of these places it may appear in physiological excess, as in the skin during pregnancy; or it may appear locally as freckles, in pigmented moles and some tumors. In other places it is not made out by unaided vision, as in muscles and sweat glands. Microscopically it appears as small grains or balls, or in plates or needles, and varies in color from pink and light yellow to red, brown and black. Its seat is either in cells or in the basement substances and may be limited to one kind of tissue or generalized. Special cells of the skin which carry pigment are called *chromatophores.*

FIG. 8.




BLOOD PIGMENT. (*Ziegler.*)

*A,* Cells containing amorphous pigment; *a,* in larger, *c,* in smaller particles. *B.* Needles and rhombic tables of hematoidin.

*Hemoglobin,* a proteid substance containing iron, is the coloring matter of the red blood cells. From this many of the other pigments are derived. Methemoglobin is produced by the action of poisons on hemoglobin, as potassium chlorate, amyl nitrite and others. In the gross the blood is chocolate colored.

*Hemosiderin.*—This pigment is derived from the red cells (hemoglobin, methemoglobin) whenever blood is destroyed in circuit or outside the vessels. It occurs as yellow, orange or red grains and differs from normal hemoglobin in its reaction

to microchemical tests; treated with potassium ferrocyanide and hydrochloric acid it turns blue, with hydrogen sulphide, black. It occurs in small extravasations, thrombi, in the malarial plasmodium, and, by its destruction, free in plasma and tissues, and in the liver in pernicious anemia. Absorbed after hemorrhage and deposited in lymph nodes, spleen and kidney it forms blood-pigment metastases. In contact with sulphur compounds, as in suppurating wounds and, after death, in the intestine and peritoneum, it becomes black and causes pseudomelanosis.

*Hematoidin.*—This derivative of blood coloring matter appears in fine granules or crystalline needles and stars. It is yellow or red, soluble in ether, chloroform, and carbon bisulphide, insoluble in water and alcohol and gives no iron reactions. With sulphuric acid it gives the color play of bile pigment and chemically it is isomeric with bilirubin. In the tissues it is found in cells and outside, in the central portions of blood masses which have been extravasated and in various organs by metastasis. Both these hemoglobin derivatives are deposited in spleen, lymph nodes, kidney and liver and may be recognized in the gross by the resulting gray or black hue of the organ; they are excreted by the kidneys and the alimentary mucous membrane.

*Hematin* is found where blood has been acted upon by the secretions of the stomach and the pancreas; hence in the feces after hemorrhages in the alimentary canal, or with diet rich in blood. It is amorphous and of a brown or blue-black color. Hemin occurs in microscopic crystals, called Teichmann's, after the action of HCl on hematin. This is a test employed in medico-legal inquiries.

*Hemofuscin* is an iron-free pigment found especially in the muscular layers of the stomach and intestine. In necropsies on the bodies of hard drinkers the pigmentation is frequently well marked in the gut. It may be due to destruction of the red cells by alcohol. General pigmentation of the body by

red-cell destruction is called *hemochromatosis* and may sometimes be recognized during life.

*Malarial pigment* resembles melanin, and consists of black, light brown, or yellow, amorphous granules, which are found in both the plasmodium and the blood and organs of the patient. *Lipochrome* is the yellow coloring matter of fatty tissue and of corpora lutea and chloromata. *Chloroma* is the name given to certain yellow or green sarcomas and as the pigment acts somewhat like fat it is probable that it is an altered lipochrome.

*Melanin* is a dark brown or black amorphous pigment formed in certain tumors, especially sarcomata developing in parts of the body normally containing pigment; by metastasis of the tumor the pigment is carried to various organs. It may be derived from the blood, but has been thought to be the product of activity of the cells involved, on account of the presence of sulphur in appreciable amount. The term covers more than one kind of pigment, some of which is due to cell metabolism, some is free from sulphur and iron, some contains either or both. *Ochronosis* is the name given to the dark yellow or brown coloration of cartilage, tendinous insertions, atheromatous plates and lymph nodes in old persons; the pigment is free from iron and lies diffusely in the tissues.

Discoloration of the tissues by biliary pigment is called *icterus,* and is due partly to the imbibition of dissolved bile pigment, partly to the deposit of granules, and with the latter there may be biliary acids in fine needles. Bile pigment is manufactured in the liver from the hemoglobin, its iron being disassociated, and is twofold, bilirubin, identical with hematoidin, and biliverdin, an oxidation product from the first. The liver is the only place where bile pigment is formed and hence jaundice (icterus), is only hepatogenous and not hematogenous. Even when poisons circulate in the blood and disorganize it (toluylendiamin, arseniuretted hydrogen, after anesthetics and transfusion, snake bites, etc.), the icterus develops from biliary stasis. During life the icteroid hue is chiefly noticeable

in the conjunctivæ, general integument, and sweat, but the pigmentation may occur anywhere except in the cerebrum, and even there in icterus of the new-born. In the urine the converted hematoidin occurs as urobilin and may be recognized by special tests.

Cutis aenea in Addison's disease, the pigmentation with atrophy regularly observed in heart, adrenals, kidneys and testes in advanced age, and similar changes in various cachexias are instances of general impairment of bodily function and constitutional decline, and are probably all connected with dyscrasia of the blood-producing organs with consequent excess of pigment in the circulation and passive deposit.

**Degeneration and Necrosis.**—Local disorders of metabolism involving tissue death are grouped under two main heads, degeneration and necrosis. The former includes all cases involving cellular death, often but one kind of cell in a mixed tissue showing the alteration, and the latter those which involve death of the tissue in mass without distinction of kind.

| THE DEGENERATIONS ARE: | THE NECROSES ARE: |
|---|---|
| Cloudy, | Coagulation, |
| Fatty, | Caseous, |
| Hydropic, | Liquefaction, |
| Hyaline, | Fat, |
| Mucoid, | Of bone, |
| Colloid, | Hemolysis, |
| Amyloid, | Sphacelation, |
| Bone caries. | Gangrene. |

*Cloudy Swelling.*—This form of degeneration, also called granular or albuminous, begins as a collection of fine granules in the cell protoplasm, giving it a turbid non-translucent look, and at the same time the cell becomes swollen, so that its normal appearance is lost; the granules are insoluble in ether, soluble in acetic acid, and alkalies, and hence resemble albumin. Such changes are sometimes associated with inflammation and sometimes are the first stage in a fatty degeneration. In the

gross an organ so affected, as the kidney, is usually swollen, the cut surface when released by the knife bulges up and the look of the tissue is opaque, as if cooked; hyperemia may be present also. Microscopically the refracting granules appear, the cells are large, there may be vacuoles, the nucleus is normal or at times involved, or the entire cell may have lost its staining powers. Cloudy swelling is common after diseases with high temperature (typhoid, variola, diphtheria) and in certain poisonings (arsenic, phosphorus, mineral acids), and from bacterial invasions. Three elements enter into the process, an imbibition of fluid, increase of supplied proteid, or the conversion of the cell protoplasm into granular precipitate; the latter source of the granules is the more probable and the process is strictly a degeneration with loss of the normal cell structure. The organs which present the change most clearly are the muscles, the liver and the kidney.

*Hydropic degeneration* is closely allied with the former as that is with the fatty variety. It is observed in cells which have imbibed fluid from the surrounding tissues, as in the case of epithelia, the cell contents being pushed aside and the space occupied by clear fluid so that the nucleus presents at one side like the seal on a ring, and the resemblance to plant cells is marked. In muscle the fibrillæ are pressed apart and the cut section has a finely frothy appearance; in time the fibrils liquefy. Such hydropic changes are different from passive edema, for in the latter case the cell may lose the fluid and return to the normal, which can not happen in this form. It occurs in inflammations and tumors.

*Fatty Degeneration.*—Normally the fat in the body is introduced in the food and drink, and it is supposed that the body has the power to manufacture it from vegetable fat, adipose tissue of the lower animals, starch and sugar, and also from proteids, though the details of the last source have not been worked out and its existence has been denied. It is said that a proteid may be split into two bodies by the cell, one holding

nitrogen and ending in urea, the other a carbohydrate from which fat may be formed as from ingested carbohydrates; normally such fat is then oxidized and disappears. Fatty degeneration would then be persistence of fat formed at the expense of the cell protoplasm. In fatty degeneration of cells, one of the most widely distributed forms of cellular death, the change from proteid to fat is supposed to occur within and from the protoplasm of the cell. (Such a degeneration is sometimes badly termed "necrobiosis.")

Macroscopically an organ affected with fatty degeneration may be somewhat larger than normal, but more often it is distinctly smaller, for we have to do with degeneration and atrophy and not the addition of something to an organ of normal size. This alone would serve to distinguish the condition from simple infiltration, but in addition the entire organ is usually involved, not certain zones of it, the fat is scattered throughout in smaller granules, and the same irritation or toxin which caused the change in one parenchymatous organ has produced similar changes in others. Under the microscope the fat is in fine granules and droplets, or of irregular size, invading all cells of one kind impartially. It is highly refracting, soluble in ether and alcohol and stained with osmic acid and soudan III. as elsewhere. When the degeneration has attained a high degree of the cells are broken up into detritus and the organ shrinks. Epithelia, connective tissue and muscle may be affected, the heart, kidney, liver and nervous organs especially. The change is due to interference with cell nutrition; hence it follows local and general anemia, great loss of blood, various poisons as camphor, arsenic, phosphorus and some fungi, diphtheria and tuberculosis; after acute diseases with high temperature the change may be due in part to the fever and in part to the special poison of the disease. In new growths of normal tissue or in tumors, and associated with both cloudy and hydropic degeneration, fatty changes in the cell

are common. Extreme degrees of infiltration sometimes pass over into degeneration.

With the fat in the degeneration last described there may also be crystals of fatty acids, the bodily fats being combinations of glycerine with margaric, palmitic and oleic acids. We may find also thin rhombic plates of cholesterin, which is normally present in myelin, bile and the blood, and occurs at times in the urine. It is soluble in boiling alcohol and ether; with sulphuric acid it turns violet or red. It is probably an intermediate product of albumin catabolism.

*Hyalin Degeneration.*—As in many of the other degenerations, the name comprises more than one kind of altered proteid, and the distinction is chiefly physical and not chemical. Hyalin is clear, glassy, homogeneous and refractile; it contains nitrogen and can be turned into sugar by boiling with dilute acid, reducing then the copper in Fehling's test. It stains by the acid anilin dyes (acid fuchsin, eosin, magdala red), less by the basic and at times by fibrin stains; insoluble in water, alcohol, ammonia solutions and weak acids. It does not respond to iodin. Several varieties are found, including that formed from epithelium, *keratohyclin;* that called *conjunctival* or secretory from connective tissue; *henial* as formed in thrombi; *inflammatory* in exudates or serous membranes, in renal tubules; and the *hyalin of tissue necrosis* in tubercular and other coagulated areas.

The source of hyalin is cell protoplasm, especially in endothelium and in leucocytes, from which small granules of it escape on treating it with hydrochloric acid; and while it has been compared to proteid altered by heat, as in cooking, it differs from that form of coagulated albumin by its insolubility.

The site of the material is either intracellular, as in coagulation, or extracellular, extruded from the cells or coagulated from the lymph between them. It is particularly noted in connection with blood-vessels, as in the walls of aneurysm, in sclerosed arteries, in endocarditis and the thickened cardiac valves,

in small arteries of lymph nodes and the mucous membrane affected by diphtheria. Collections of extravasated blood often undergo hyalin degeneration. It is found on the chorionic surface of the placenta, and a variety of it develops in the muscles during protracted diseases with great temperature variation, as typhoid. Blood plates and leucocytes undergo the change in some diseases and form hyalin thrombi and emboli in arterioles and capillaries; tubercular masses, gummata and certain tumors, especially endotheliomata, also become hyalin as part of a regressive change. It is often not the only form of degeneration present, being combined with fatty and calcific, or closely related to fibrinous and necrotic coagulation and at times the first stage of amyloid.

In the gross there may be nothing noticeable, as the hyalin is often confined to the walls of the smaller vessels; or the part may be dense, increased slightly in volume, pale, at times containing minute vitreous scales, and if a precursor of amyloid giving the iodin reaction. In muscle the tissue is reddish yellow, semiopaque and lustrous, and friable; on mucous membranes small false membranes are found or slightly swollen submucous plaques.

Microscopically it may appear in spheres and granules, or as a homogeneous mass, the nuclei of the part staining feebly or not at all, as in cerebral membranes, plexuses and tumors and the pineal body. A granular form occurs in leucocytes, which may perhaps be regarded as monocytic glands, and from them can be recovered with acid as above. In vessels it appears in any of the coats and affects the smaller arteries first. There is a supposed relation between this degeneration and cells derived from the mesoderm.

*Mucoid Degeneration.*—The degenerated matters embraced under this head are nitrogenous, derived from albumin, swell in water and then dissolve, are precipitated by alcohol and acetic acids and not redissolved in excess of the same, are soluble also in neutral salt solution, caustic alkalies and alkaline

carbonate solutions; they are not diffusible, being compounds of animal gum and albumin, hence called glycoproteid; they contain nitrogen and sulphur. They fix best in corrosive sublimate solution, take hematoxylin feebly, basic stains better; thionin and toluydin blue best. With dilute acid and heat they make sugar and react to Fehling's test, except synovial mucin; paramucin reduces copper without previous boiling with acid.

Two varieties are recognized, *mucin,* from the submaxillary, intestinal glands, tendons, etc., which has the qualities given, and *pseudo-mucin* which is not precipitated with acetic acid and sometimes appears refractory to sugar tests. But this second kind includes paramucin, metamucin, and perhaps others and is merely a name for all mucin which differs from the typical form.

The normal type is found in the mucous glands, umbilical cord, bursæ, tendons and synovial membranes and is either jellylike or stringy, translucent and viscous. Pathologically it is to be recognized in two forms, (1) the excess accompanying inflammations of mucous surfaces, poured out of the beaker cells in unwonted volume and hence thinner than normal, or collected in a thick layer on a mucous surface chronically diseased and having no apparent inflammatory reaction under it; and (2) in the form found in the tissues where it never appears normally, as in cartilage and bone marrow. In discharges from the genito-urinary passages the fluid sometimes contains nucleo-albumin in large amount; if this were retained it might proceed to complete mucous degeneration and points to a common source of mucin.

The site of mucous degeneration is chiefly the mesodermic basement substance between cells; it occurs in connective tissue, as cartilage and fat, in marrow, in sarcomata and cysts; in bone the calcium salts disappear first and then the mucin appears. It occurs also in masses of pus cells. In cavities it collects as a thick clear fluid, afterward thinner, or it may be mixed with pus cells and colored by blood pigment; the

amount may be large, as in the gall-bladder and the normal epithelium atrophies from pressure.

Microscopically in mucous membranes the goblet cells are more numerous and larger than normal. In the healthy condition their function does not involve their death, in the inflamed it does; inflammatory reaction coexists in acute cases. In the tissues there is partial or complete absence of basement tissue, mast cells are at times abundant, the vessels usually escape, and there may be small cysts.

*Colloid Degeneration.*—In this the material strongly resembles mucin in appearance, but with alcohol and acetic acid it merely swells, resembling pseudo-mucin; it is firmer and more consistent, mucin resembling mucilage among adhesive substances and colloid resembling glue; it does not involve interstitial structures but is confined to cells. Its dryer nature is seen in its shrinking and cracking at times. Amyloid reaction not given. It takes acid stains and becomes red with picro-fuchsin. It may stain by Gram's and Weigert's methods.

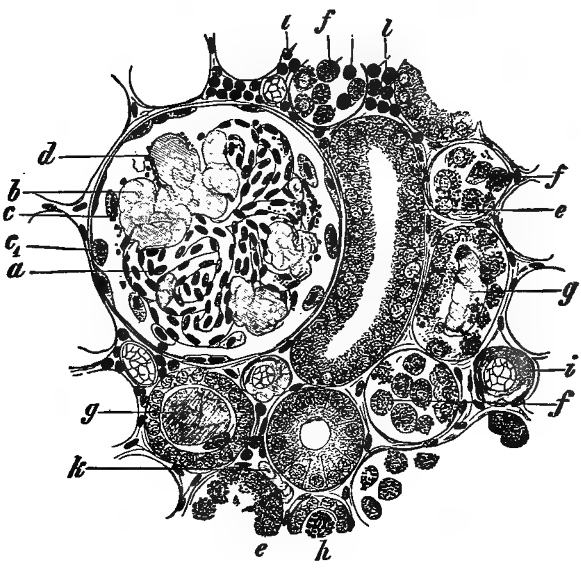
Colloid material may form in both epithelial and connective tissue cells; normally it is found only in the thryoid. In the form of degeneration it begins as small points in the cell body, refractile and homogeneous, which increase till the entire cell is involved, the nucleus either atrophied or also turned into colloid. Several of these fuse and sometimes make relatively large spheres which may be marked by radiate and concentric lines corresponding to the age of different layers and consequent shrinking in the older and dryer. Where a tissue holds many such areas they often communicate with one another in a coarsely reticular manner. It is found in long mucous glands, as in the uterus, in renal tubes, the adrenal bodies, the hypophysis, in great quantity in the hypertrophy of the thyroid gland, in the prostate at times and in many degenerated tumors.

In the gross there may be small areas like swollen sago through an organ, yellow and glue-like, with increased density of the part; single and multiple cysts may be present; some-

times there are laminated concretions. The cysts may contain blood, pus, cholesterin tables and crystals of calcium oxalate. Edema often coexists.

Microscopically the gland cells throughout the acini are involved, there is anemia of the tissue, and the swollen part may

FIG. 9.




AMYLOID KIDNEY. (*Ziegler.*)

*a*, normal vessels of the glomerulus; *b*, vessels which have become amyloid; *c*, $c_1$, fatty epithelia; *d*, fat lying in drops on the glomerulus; *e*, fatty epithelium in urinary tubules; *f*, the same, desquamated; *g*, hyaline cast; *h*, fatty cast; *i*, amyloid change in vessel wall; *k*, amyloid capillary; *l*, cellular infiltration of connective tissue.

exert pressure which atrophies other cells. The crystals and onion-like bodies are found as mentioned above.

*Amyloid Degeneration.*—Of the albuminous degenerations this is the most important clinically because of its effects on the

general condition, although a tissue involved in any of the albuminous degenerations is probably beyond recovery; and yet it does not so often come to the notice of the pathologist in modern times because of the great advance of surgery and the infrequency of the long suppurative processes which used to be tolerated. Amyloid material is glassy, colorless or slightly yellow, firm and somewhat elastic. With iodin tincture, alone or combined with potassium iodid, it turns mahogany brown; on adding chlorid of zinc solution or sulphuric acid it becomes blue to violet; with methyl violet (iodomethylanilin) it stains red, normal tissue being blue-violet. Because of the reaction with iodin amyloid obtained its name (meaning "like starch"), and was considered an animal cellulose and hence a carbohydrate. It is now known that it contains nitrogen and is albuminous, though it differs from albumin in its reaction and in resisting chromic acid, alkalies, alcohol and ferments (pepsin, putrefaction); but pure and in powder, pepsin and weak hydrochloric acid digest most of it, the rest being nuclein. Trypsin digests it and sulphuric acid splits it into leucin and tyrosin.

Amyloid is therefore a degeneration product, without a type in the normal body, the result of nutritive changes in proteids. It appears in the body after chronic suppuration and diseases accompanied by it, tuberculosis of lung and bone, syphilis, ulcerating carcinoma, varicose ulcers, etc., and may occur also in chronic dysentery, leukemia, typhoid and actinomycosis; occasionally it occurs in the child without any such chronic disease as an antecedent. In all these cases we are justified in referring the product to the unexplored territory of the pathological ferments.

Its site is frequently in the walls of arteries and capillaries, the endothelium not affected, the lumen being quite or nearly closed; usually the media and intima are the site of its appearance, less often the adventitia; it may be irregularly distributed along the course of the vessel in rings and diamond-shaped patches with wide normal intervals between. In the lymph

nodes and the spleen it attacks the connective tissue and the capsule is often thickened. In the parenchymatous organs of man it is usually confined to the interstitial structure, in some of the lower vertebrates it may involve the cells also. Gland cells suffer passively or degenerate from interference with nutrition and become fatty. At times it follows hyalin change and involves the same parts.

In the gross the appearance differs according to the amount of the change and its locality; if confined to small vessels it may not be visible. Otherwise the part is swollen, dense, elastic, increased in weight, the form is not distorted, pale from its anemia, dull and glistening on section, translucent in thin section, and with a peculiar look which has given its name of "waxy" degeneration. Many organs may be involved at once, especially the liver, kidney, spleen, adrenals and colon. The question whether the amyloid is formed in the blood and deposited in the organs, that is, whether it is an infiltration, or whether it is the result of local variations in proteid metabolism, affecting many organs and seeming general at times, in other words a true degeneration, has the weight of authority for the latter. We recognize a reciprocal relation between cell activity pathologically disturbed and variations in supplied albumin, we suppose the presence of a ferment foreign to the organism, and explain the interstitial amyloid as partly an extrusion from the cells and partly a coagulation between them. The results of amyloid degeneration clinically are loss of function from local anemia and interference with the cell, general anemia and cachexia because so many of the chief organs are attacked, many of them occupied with blood formation. In the gut ulcers may form and hemorrhages occur from them. Its course is slow, usually through several months.

The microscopic appearances are implied in the above.

As a local manifestation amyloid occurs in granulation tissue and parts chronically inflamed, in connective tissue hyperplasia, in tumors with other degenerations and in gland lumina as

concretions. On the conjunctiva it occurs with hyperplasia of adenoid elements and resembles trachoma. In the larynx it is found in syphilitic scars, as also in lymph nodes, the liver, and in tumor-like swellings under mucous membrane. In these cases it occurs in the basement substance, at times with hyalin material, and gives the iodin reaction.

*Corpora Amylacea.*—Through the accident of a name these bodies have been supposed to be amyloid; both take their name from starch (amyl), but the degenerated material does so because of its chemical reaction and the concretion because of its concentric or eccentric markings like those on a starch granule seen under the microscope. Corpora amylacea come from the most varied sources and both normal and pathological conditions, and undoubtedly the term includes many different forms; their origin and chemical nature have not been entirely determined. They are small ovoid or spherical bodies, at times visible to the naked eye as brown grains (prostate), do not swell in boiling water, split with dilute acid nor melt in fuming nitric. Microscopically they are homogeneous if young, marked by concentric or radiate lines if older, made up of a central darker portion at times consisting of several smaller ones, which alone may be marked, and a lighter or yellowish outer zone. With iodin they may become red, or, even without sulphuric acid, turn blue or violet at once; sometimes only the central portion reacts. As they are a regular phenomenon in the degenerations of old age, it is reasonable to consider them a degenerative product everywhere; they contain phosphorus and nitrogen and seem related to lecithin. They may form from epithelium, as in prostatic lumina, or from connective tissue (endothelia) as in fibroma of the dura. They have been recognized in the following also: spinal cord, ependyma of ventricles, lung, inflamed areas, in bile and phleboliths, and in certain tumors as carcinoma.

*Caries of Teeth and Bone.*—Although quite different from the degenerations already described, yet, as the only molecular

death which osseous tissue can suffer, caries belongs in this group; it will be treated at length in the division of Special Pathology, p. 639. In caries the bone cells become fatty or granular, the basement substance is absorbed or degenerated into mere detritus, or the lime salts are extruded and the basement substance becomes fibrillary and atypical and undergoes fatty degeneration. Suppuration is commonly associated with the caries.

**The Necroses.**—Distinguished from death of the individual cell, singly or in groups, or of the basement membrane, neither of which may destroy the function of the part at first, and from which it is possible for an organ to recover if the process can be arrested or ceases of itself, we have the various forms of necrosis. These stop function at once and permanently and from them there is no recovery for the part, though the organism as a whole may slough off the diseased portion or wall it in by fibrous tissue and lime incrustation.

The distinction is partly of one degree, necrosis being always a worse condition for the part, destroying it totally, than degeneration of one of its elements. It is partly also a distinction in kind, for although degeneration often leads to necrosis and is combined with it, yet certain forms of necrosis are clearly separated from other pathological processes. The name is applied to massive death of normal tissues and similar changes in neoplasms and inflammatory products.

If grouped according to cause we have two main divisions, those due to disordered cell nutrition and those due to injury, and the results vary according to the patient's age, health and ability to resist disease, the integrity of the blood circulation in the part and hence its temperature, the condition of the lymph stream, the activity of the cause and the duration of its influence, the presence of other diseases and idiosyncrasy. The following scheme of the causes will make the subject clear:

- Necrosis
  - Disordered nutrition
    - through circulatory system
      - anemia
      - stasis—blood and lymph
    - through nervous system—vasomotor and reflex
  - Injury
    - Mechanical
      - violence, pressure, tension
      - extremes of temperature
    - Chemical
      - poison
        - acids
        - alkalies
        - metals
      - parasites
        - animal
        - bacterial

It is perhaps seldom that one cause acts alone; commonly two or more act together or one acts in more than one way, and the whole is accompanied by infiltration, degeneration or both. In other words the condition is very complicated and the descriptions and subdivisions on paper are a device toward comprehension.

The various tissues are not equally susceptible to the causes of necrosis; as a rule the more highly specialized are destroyed first, and a rough scale may be given thus, the less sensitive last — gray nervous tissue, white ditto, gland cells as kidney and liver, epithelium, muscle cells, blood-vessels, connective tissues. The result of necrosis is removal of the part either by absorption, or if on a surface, sloughing, and partial replacement by scar tissue, or failure of such repair and ulceration remaining, partial separation from the body, as sequestrum, encapsulation and cyst formation.

A good example of necrosis from anemia is found in the production of an infarct from embolism, the part deprived of its nutrition at once becomes anemic and dies. More gradual change of similar nature is seen in gangrene of old age, the diminished lumen of the arteries with weakened heart action slowly depriving the part of its nutrition and setting up dry

gangrene (mummification of the foot). Inflammatory exudation, as between periosteum and bone, may cut off the nutrition and lead to necrosis. When the venous return of a part is stopped, as in hernia incarcerated by a tight ring, it suffers passive congestion from which it is possible to liberate it for a time; after that, death follows inevitably as local gangrene. Mechanical influence, crushing and similar injury, acts partly in complete destruction of the cells at once, and partly such injury to the vessels of the region that nutrition cannot continue. Since lighter grades of the same thing may cause inflammation, we often find necrosis and inflammation in different areas of the same organ, and in the effort to remove a necrosed portion, inflammation is one of the chief factors. Heat and cold if extreme kill the tissues at once, and usually those which lie at a distance from the heart and have relatively little blood. When foreign bodies distend the wall of the canal in which they lie, they may interfere with nutrition and lead to perforation; this occurs with biliary calculi. In connection with this there may be other influences, as when gases and bacteria from the intestine join with foreign bodies in some part to weaken and perforate the wall. Corrosive poisons act either by destruction of the part touched, removing its water and making new combinations with its elements, or by destroying the circulation; and perhaps the action of bacterial toxins, as in diphtheria, is partly of the same nature. Some infections constantly invade new territory, with increase in the number of the germs and of their products, and thus a gangrenous process migrates. In some cases gas is produced in quantity in the tissues (as from bac. aërogenes capsulatus) and local emphysema results, the pressure and the nature of the gas aiding in the death of more tissue. Necrotic processes may pass from place to place interruptedly, as when a middle ear suppuration causes septic thrombosis of a cerebral sinus and an embolus from here sets up gangrene of the lung. Necrosis, sepsis and inflammation may thus be closely related.

Microscopically the cells in a necrosed part remain as ghosts which do no take stains, or are destroyed beyond recognition. The cell body loses its normal granulation, becomes cloudy, its protoplasm breaks up, vacuoles form, hyalin changes may occur; if in lymph, edema sets in and the capsular membrane may burst and set the altered elements free. The nucleus may merely lose its staining power or break up (karyorhexis), or its chromatin may be altered and in part removed from the nucleus (karyolysis) and cell and nucleus dry up to an indifferent scale. In these changes the flowing of the lymph stream through the cell is supposed to play an important part, while the cell elements are passive. The basement substances are variously degenerated and liquefied, contained lime salts, as in bone, being reduced to little collections of mineral grains or dissolved and removed.

The various kinds of necrosis (grouped mainly according to gross appearance) are:

Coagulation necrosis,
Caseous necrosis,
Liquefaction necrosis,
Of fat tissue,
Of bone tissue,
Of blood (hemolysis),
Gangrene.

*Coagulation Necrosis.*—When a part is dead or dying and is still bathed in tissue lymph, this fluid may coagulate either between the cells or within them. If outside the cell there is coagulation within and about the blood-vessels, inflammatory and other ex- and transudates, and this may be observed on surfaces, as mucous and serous, or in the tissues, the result being fibrillar or hyalin or granular coagula. In the cells the nuclei are lost, the body is granular or hyalin, and after a time the cell breaks up into detritus and is removed. This form results from embolism and thrombosis, from the effect of pus, tubercle and diphtheria organisms, and from high temperatures; certain

chemicals coagulate the proteids in the tissues, as carbolic acid, leaving them firm and rigid. The part may become caseous, cast off or dissolved by suppuration, or enclosed by fibrous tissue and the latter infiltrated with earthy salts. In the gross the part may be firm, larger, gray or yellowish. Microscopically the nuclei may retain a slight degree of staining power or none. Weigert's fibrin stain shows fibrils and grains of fibrin; all elements are involved including pus and red cells. It is closely related to fibrin coagulation though at times the fibrillæ do not take stains.

*Caseous Degeneration.*—This is but a variety of the first kind, but it occurs so frequently in tubercular disease that it may be mentioned specially. The coagulated area is yellowish, dry and firm, a large element of fatty degeneration associated; or it is of lighter hue, softer and creamy in consistence. It may occur in syphilitic growths and in tumors. The degenerated cells and fibers, often mixed with fibrin bundles, take up fluid and become more or less liquefied, and may then be absorbed; or drying proceeds, lime salts deposit and a fibrous capsule forms. Such areas are common in the lung where they are called areas of "healed," or better, latent tubercle.

*Liquefaction Necrosis.*—Where a part is not well supplied with coagulable albumins, but is bathed in fluid, necrosis occurs as a quasi-digestion of the elements and the result is a fluid which holds cell detritus in suspension and is variously colored by biliary or blood pigment. If later there is an addition of proteid from blood or lymph, the process passes over into coagulation necrosis, just as that form may liquefy, and the probable presence of ferments in the part makes the resemblance to digestion very close. Such areas are frequent in the brain and the cord and are known from their color as red, yellow, fatty, and other softenings; in old and partly absorbed cases the color is deep yellow or ochreous. Other cases are stomach digestion of a coagulated area and resulting ulcer, burns with blebs and vesicles where the cells necrosed by heat

are digested in the fluid; and in the secondary form it occurs in tumors, inflammatory products, and caseous areas.

*Fat Necrosis.*—This form occurs in the fatty and other tissues of the abdomen, usually about the pancreas, and may be traced to the escape of pancreatic fluid, usually by transudation, when the normal flow of the secretion into the intestine is hindered. Thus when the pancreatic duct opens by its own papilla (duct of Santorini), apart from the common bile duct, a calculus lodging in the ampulla could produce only biliary stasis. When the two ducts open in common, inflammatory swelling of the papilla, calculi in its lumen, and perhaps other mechanical conditions may produce pancreatic stasis; the fluid transudes from the ducts, possibly also from the acini, into the surrounding tissue, either as a whole or in part. The fat-splitting ferment, steapsin, thus attacks the peri-pancreatic fat, and in early cases the change will be found there only. Later the fat in more distant situation is attacked and also the pancreatic tissue and vessels. A small piece of human fat, stroked with a piece of fresh and normal human pancreas, and kept in a moist chamber at body heat, will show similar fat necrosis after twelve to twenty-four hours. (See Pancreas, p. 489.)

As found in the cadaver the tissue affected with fat necrosis is speckled with small, grayish points, about one or two millimeters in diameter, or they may be microscopic, which do not pierce the tissue very far in most cases and which may feel rough on palpation. Under the microscope these areas are necrotic, sometimes contain crystals of fatty acids, sometimes combinations with lime which stain intensely with hematoxylin. There is often active inflammatory reaction about them. If the process persists and invades the blood-vessels death may follow from hemorrhage, behind the peritoneum or into its cavity.

*Necrosis of Bone.*—When the nutrition of a bone is interrupted by embolism, by stripping up a periosteum, or by the effect of chemicals, especially phosphorous, a larger or smaller

mass of it dies and the process is called necrosis. The dead portion is separated from the healthy by a line of demarcation, and extruded or retained in apposition. The dead piece, called the *sequestrum,* is variously eroded by the tissue juices and may be on the outer or the inner aspect of the bone, usually external and in bones of the limbs. In other words, this is a form of gangrene and differs from that of soft parts because of the peculiar nature of the tissue.

*Hemolysis.*—Various chemicals, as carbon monoxide, hydrocyanic acid and its salts, and hydrogen sulphide stop the chief function of the red cells, oxygenation, and thus may be said to cause their death; the blood being regarded as a tissue rich in cells whose interstitial substance is fluid in health, and which is all the more complicated because it contains both nutriment for other tissues and products of waste. Other poisons destroy the red cell and liberate its coloring matter, causing *methemoglobinemia,* as ozone, chlorates, pyrogallic acid, acetanilid, and many others. In malaria, relapsing fever and some other diseases similar effects are seen. Since a marked degree means death of the patient it differs from other necroses, but the cells, both white and red, and the plasma, are altered and functionless, dead in other words, and strictly the case may be an example of necrosis. (See also Immunity, theory 6, p. 240.)

*Gangrene—Necrosis with Putrefaction.*—Any necrosed area, by the entrance of saprophytic bacteria, may begin to undergo the process of proteid decay, the continuous chemical decompositions and rearrangements which soften and finally liquefy the tissues, with the production of gases, and resulting water, carbonic acid gas and ammonia as the end products. In the course of the process many temporary nitrogenous compounds are formed which resemble alkaloids and are highly poisonous to the organism. The microörganisms are many, from fungi to spirilla, and succeed each other in groups after a fairly regular order, but usually there are those present which produce gas.

Gangrene occurs in two chief forms, moist and dry, the former where the tissues are still supplied with lymph and the latter where they simply mummify; in the former emphysema is more common than in the latter. A small portion of another and larger part, if gangrenous, is called a *sphacelus* or *slough*. Where either form occurs in the old from weak heart and diseased arteries it is called *senile gangrene*. Where no cause can be discovered but eating rye flour which has been spoiled by claviceps purpurea (the source of ergot), it is called *raphania* and frequently has broken out in epidemic form. *Toxic* and *infectious* gangrene are terms which explain themselves. *Neuropathic* gangrene is partly the result of disordered nutrition, as from pressure over a bony prominence, and partly the result of disordered innervation; this occurs most commonly as *bed-sores*. Other examples may be found in *perforating ulcer* occurring in disease of the cord, *symmetrical gangrene* (Raynaud's disease) of distal portions of the body, fingers, toes and ears, *joint lesions* in locomotor ataxia, etc., where blood supply is probably also a factor. Beside the local process in gangrene the absorption of nitrogenous products (ptomaines) and entrance of bacteria into the general circulation are of great clinical importance.

## Appendix to Chapter V. Death: Post Mortem Changes.

The definition of death must be so broad as to apply to all living things, and, as the essential thing in life is function, it must refer to that. Anatomical, that is, structural changes follow, or if they precede are not fatal till function ceases; thus when both lungs are nearly solid from lobar pneumonia and the patient breathes with only a small part of one, he is still alive until the function of respiration stops, and the anatomical condition may even be on the road to recovery. Hence death is that condition of an organism in which further metabolism is impossible.

The three essential functions are respiration, circulation and innervation. Other functions however important may, and normally do pass through periods of quiet, these three never pause during life. Respiration may be reduced to one or two a minute, as in opium coma, circulation may fall to thirty-five heart beats or less a minute, and innervation be so disordered that the other two are irregular, intermittent and too feeble to be discerned, but metabolism goes on, no matter how little, and while that is possible there is no death. When the boundary is passed beyond which metabolism cannot be reawakened, at that instant somatic death occurs, but in the majority of cases it is impossible to say at what second this happens. Death may occur at an advanced age through apparent failure of all the bodily powers, and statistically this accounts for about 6--8 deaths per thousand living. At any other time of life we require an explanation of the cause or at least the manner of the death, and the causes of disease already given are also causes for some deaths. Obviously an organ which has had to work harder than normally, as the heart in chronic cardiac disease, reaches a condition of senility before other organs and is exhausted before general old age; and a tissue which has suffered from a chronic disease will be less resistant to another, so a lung in tuberculosis is easily affected by lobar pneumonia. Or the destruction of tissue may not leave enough for normal function, as when a kidney is atrophied by the pressure of hydronephrosis. In many cases death is clearly secondary, as in the kidney cited, where destruction implies retained excreta and uremic poisoning, or when several diseases coexist and it requires trained judgment to decide which lesion was fatal.

The function and organs of locomotion and reproduction (as also the special senses) may be lost without danger to life; intestinal and hepatic functions may be stopped for several days and still death is not inevitable; renal function may cease for many hours; but the patient dies from failure of respiration,

stoppage of the heart or lost innervation. Death may occur, then, by asphyxia, by syncope, or by coma.

Death may be sudden after injury, loss of blood, severe mental shock, or when the body is overwhelmed by poison, as in carbolic acid poisoning and fulgurating cholera; or it may be protracted through a series of years, as in locomotor ataxia, part after part becoming useless and function after function lost, till disease involves function essential to life, and life ends.

The appearance of the dead body varies according to its blood content, the length of time dead, the cause of the death, and the temperature of the surrounding medium. After great hemorrhage the surface is pale. If the blood is present it settles to dependent portions (*hypostatic congestion*), as the back, the lowest parts of the lungs, the spinal canal and back of the skull; when the body has lain prone corresponding lividity of the anterior half is noted. The blood is still in the vessels, for wherever pressure has been exerted it is mechanically squeezed along, leaving anemic areas. It gathers especially in venous radicles and remains fluid. The little that persists in the larger vessels tends to clot. The post mortem lividity is cherry red in poisoning by carbon monoxide. After death the bodily temperature may rise for a few hours, perhaps explained by terminal infection and great bacterial activity, but usually it begins to fall at once and loses about one degree an hour till the surrounding temperature is reached. The skin loses its elasticity and tension and where pressure has acted the body is flattened; if hyperemic before death the skin may not be so afterward, and thus most skin eruptions disappear post mortem. Where the skin has been rubbed and the epidermis removed the area becomes dry, hard, semi-transparent, and looks as if varnished; the conjunctiva also dries and becomes darker and the eyeballs lose their tension.

The albumin of the muscles coagulates (formation of myosinogen within the sarcolemma; then myosin and muscle serum), it becomes acid (formation of sarcolactic acid), gives

off carbonic acid and is shortened and diminished in volume and friable.* The beginning of these changes is accompanied by rigidity, *rigor mortis,* which begins at once or a few hours after death in the intrinsic eye muscles, then the jaw and neck, upper extremity and thorax, abdomen and lower extremity, lasts a few hours to days and passes off as it began. If developed slowly it usually lasts longer. Smooth muscle is affected as well as striated, hence cutis anserina from rigid arrectores pilorum.

After a longer time the superficial veins are marked out as a wide, dark red meshwork from imbibition of blood coloring matter. Putrefaction has begun where sulphur compounds ($H_2S$) and bacteria are found, as in cecum and ascending colon, and the action of the sulphur on the hemosiderin makes sulphid of iron; because this is black and is seen through the yellow skin the effect is greenness of the abdomen. Putrefactive odors are present and the contents of the alimentary canal are pushed out by the forming gas, into the trachea, out of the mouth as a dark froth and out of the rectum. The tissues soften, epithelial and glandular first, connective last; fat from the liver may be driven up into the lung, as also clots from the right side of the heart, by the pressure of the gases; superficial parts become swollen, black or green, emphysematous, hair and nails fall off. Warmth and moisture favor the rapidity of the changes, and they occur quickly in the obese and in infants, after the puerperal state and infectious disease; cold, leanness, poisoning by alcohol and arsenic, etc., retard them.

Apparent death occurs when metabolism is reduced to its lowest terms and it may be a matter for careful investigation to determine if circulation and heart beat, respiration, and innervation even in the deepest reflexes, have disappeared. In

* Recent study tends to show that there is no such acidity, coagulation, nor shortening; and that the lowering of temperature is the chief factor in producing rigor mortis.

doubtful cases the body should be kept till positive evidences of putrefaction appear, and of course without embalming or other preservative measure. Apparent death may occur in catalepsy, cholera, electric discharges, hysteria, asphyxia, submersion and after exposure to cold. The usual tests are — ligature round finger, notice if swelling occurs distally, or blood flows from a puncture; mirror held to lips, collects moisture if respiration present; tissues illuminated, as the fingers held together and a strong light back of them, reddish look if blood present, pale if absent; electric discharge to excite reflexes; X-ray examination of heart and lungs to detect movement.

- Disordered Metabolism
  - Constitutional (Chap. IV)
    - Amount of Pabulum
      - Excess
        - Overfeeding
        - Plethora
        - Obesity
      - Defect
        - Inanition
        - Starvation
        - Cachexia
    - Use of Pabulum
      - Anabolic
        - Alimentary Canal
          - Acid intoxication
          - Putrefaction in gut and auto-intoxication
          - Peptone, albumose
        - Liver and Pancreas
          - Bile in circulation
          - Fatty stools
          - Diabetes
      - Catabolic
        - Excessive waste
          - Fever, chronic disease, tumors, pus infections, Grave's, etc.
        - Disordered Excretion
          - Material lost—albuminuria, hematuria, glycosuria
          - Not excreted—acetonemia, uremia, alloxin and uric acid, etc.
    - Appendix—Fever
  - Local (Chap. V.)
    - Quantitative
      - Excess
        - Hypertrophy
        - Hyperplasia
        - Metaplasia
        - Heteroplasia
      - Defect
        - Aplasia
        - Agenesia
        - Hypoplasia
        - Atrophy
    - Qualitative
      - Tissue addition (infiltration)
        - Normal material
          - Inorganic
            - Dust
            - Lime
            - Urates
          - Organic
            - Fat
            - Glycogen
            - Cholesterin
            - Heteroplasia
        - Pathological material—Pigment; dropsy
      - Tissue destruction
        - Cellular death (degeneration)
          - Cloudy
          - Fatty
          - Hydropic
          - Hyalin
          - Mucoid
          - Colloid
          - Amyloid
          - Caries
        - Massive death (necrosis)
          - Coagulation
          - Caseous
          - Liquefaction
          - Of fat
          - Of blood
          - Of bone
          - Gangrene
    - Appendix—Death: post mortem changes

# CHAPTER VI.

## INFLAMMATION AND REPAIR.

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**Definition.**—Inflammation may be conveniently defined as the reaction of tissues to an injury.

**Etiology.**—The variety of factors concerned in inflammation is very great. The principal exciting causes are mechanical, thermal, electrical (X-ray), chemical and bacterial. While all but the last of these causes frequently act singly, exciting various grades of inflammation in direct proportion to the quantity of the agent present, bacteria seldom figure alone as a cause of inflammatory reaction. The mere presence of bacteria is seldom sufficient to excite inflammation of a superficial tissue; there must usually be secondary contributing causes, such as a wound or exposure to cold, and also a predisposition on the part of the individual. In the etiology of bacterial disease, therefore, are commonly associated (1) exciting, (2) contributing and (3) predisposing factors. Even with the simpler chemical agents, contributing and predisposing factors are often of great importance in determining the grade of inflammation.

The accurate estimate of the relative importance of exciting and contributing causes of inflammation is often an extremely important and difficult question. The grade and character of the inflammation excited by various agencies are usually of somewhat definite type; thus the result of a burn differs from the lesion caused by bacilli. It is an important fact that the first five of the etiological agents mentioned, when acting alone,

while sometimes capable of producing inflammation of purulent grade, yet are usually followed by the less intense grades of reaction, and that the vast majority of purulent inflammations are of bacterial origin. All pathogenic bacteria may, but many seldom do, excite purulent inflammation. A purulent inflammation is almost never of purely tuberculous origin.

In general bacteria excite purulent inflammations with self-perpetuating tendencies, while other agents induce non-purulent processes of self-limiting type.

## The Action of Bacteria in Inflammation.

**Mode of Entrance.**—Bacteria usually enter the body, and reach a position where they are capable of inducing disease, through passages lined by mucous membrane (respiratory, gastro-intestinal, genito-urinary). Previous inflammation of these mucous passages, or any form of lowered vitality, very greatly favor the further development of the inspired or ingested microörganisms. Through fresh wounds which may be of minute size, pathogenic and non-pathogenic bacteria often penetrate the tissues, and finding conditions favorable to their development, the former go on to induce infectious processes of varying extent.

In any case, the entrance of bacteria and their further development is often greatly favored by their association with various chemical poisons which are capable of causing degeneration, and necrosis, of lining cells.

The intact skin is sometimes penetrated through hair-follicles and sebaceous glands (*sycosis*), and some infectious agents are inoculated through the skin by the bites of insects. Thus a mosquito carries malarial infection, and a tick the disease of cattle known as Texas fever.

When infection of the blood or internal viscera occurs in the absence of any wound or abrasion of mucous or cutaneous surfaces, by bacteria which ordinarily require such aids to their entrance, the infection is said to be cryptogenic.

**Mode of Action.**—Once within the body, in mucous passages, in serous cavities, or in tissue spaces, their pathogenic action depends almost entirely upon the effects of poisonous principles elaborated by the bacteria, and only to a slight extent upon the mechanical effects of their presence.

These poisonous principles are of variable chemical nature, and are produced under varying conditions. They have been classed as follows:

**Ptomaines and Leucomaines** are crystallizable alkaloids produced from tissue-albumins by the action upon them of bacterial growth.

1. **Ptomaines** are alkaloids developed by non-pathogenic bacteria growing in dead animal matter. They occur under some very peculiar conditions and their presence in decayed flesh is often transitory.

2. **Leucomaines** are alkaloids developed by pathogenic bacteria growing in living tissues.

3. **Toxines** are poisonous products developed from tissue albumins by the growth of pathogenic bacteria. They do not form salts with acids as do ptomaines and leucomaines, and are not crystallizable.

4. **Toxalbumins** are poisonous principles thrown off from the bodies of pathogenic bacteria. These are usually specific substances, more or less peculiar to each bacterial species, and not only are developed in the living animal tissues, but have been produced by cultures of bacteria in non-albuminous media.

Toxalbumins lose much or all of their toxic properties when heated for one hour at 58° C. They do not induce toxic symptoms immediately after injection into the animal organism, but require hours or even days before giving rise to local or constitutional disturbance. They are extremely active in minute quantities. These three facts favor the view that the specific poisonous substances produced by bacteria are enzymes or ferments, but the present knowledge does not warrant a positive opinion on this subject.

While ptomaines, leucomaines and toxines, when injected into the animal organism, induce symptoms which often have little resemblance to the clinical disease set up by the bacterium growing in the living tissues, toxalbumins, on the other hand, usually initiate a train of symptoms closely resembling the clinical disease excited by each particular bacterium.

Bacterial inflammations are excited then by the effects upon tissue cells of the various poisonous principles, which by chemical action cause degenerative changes and the subsequent train of vascular and cellular processes. Comparatively little importance can be attached to the withdrawal of nourishment from local infected tissues to the growing bacteria. Constitutional symptoms are produced by the absorption of poisonous products by the blood current and their distribution throughout the system. This is called *toxemia.*

In very susceptible individuals infected by virulent bacteria, the blood stream may be invaded, temporarily and producing distant metastatic foci of inflammation, or permanently and developing a general infection of the blood, or *bacteremia.*

**Intoxication.**—When considerable quantities of ptomaines or leucomaines or of toxins and toxalbumins are ingested and absorbed, profound constitutional disturbance may result immediately without the further development of bacteria. Such a process is called *intoxication.*

**Infection.**—When the progressive development of bacteria in the body is required before sufficient toxic material is present to produce symptoms, the process constitutes an *infection.*

Simultaneous development of two or more pathogenic microorganisms is called *mixed infection.*

Certain pathogenic bacteria excite a local inflammation which occasionally offers a ready point of entrance for a second more virulent microörganism and the new germ begins at once to dominate the inflammatory process. Such an event is called *secondary infection.*

## THE INFLAMMATORY PROCESS.

The phenomena comprised in the inflammatory process are:

Degeneration of tissue cells (initial injury).
Changes in the circulation.
Exudation.
Secondary degeneration and death of tissue.
Growth of new tissue.

These phenomena occur in a great variety of combinations but the predominance of one or other of them usually gives a character to the process on which the nomenclature of inflammation is based. Each of them requires consideration in detail.

### Initial Injury.

An **initial injury** or degeneration of tissue cells appears to be an essential preliminary to all inflammatory processes. Mechanical injury may merely divide these cells in two; heat, the X-ray, chemical agents, and bacteria may cause slight or severe alteration in the life processes of the cells; but in every instance some grade of injury or irritation of tissue cells appears to precede the more readily recognizable changes of inflammation. The exact character of the changes in tissue cells resulting from the initial injury is imperfectly understood since they are of delicate nature and are rapidly obscured by other processes, chiefly by disturbances in the blood-vessels.

### Reaction to Irritation Among Protozoa.

Pure illustrations of cellular reaction toward irritating substances are found in the behavior of amebæ and various protozoa toward foreign bodies.

Observations on a multicellular myxomycete *Æthalium septicum,* and on the *plasmodium of Fuligo* have brought to light the existence in these low organisms of a peculiar susceptibility towards certain influences; this is known as *chemotaxis.*

*Æthalium septicum* is a multicellular ameboid organism which when placed on a moistened surface near a drop of infusion of oak-bark moves actively toward and into the infusion. The *plasmodium fuligo* is another unicellular ameboid organism which when placed on a moistened surface near a drop of one-per-cent. solution of salt, at first moves away from the solution, but later, especially if needing water, it will approach and enter the solution.

These observations illustrate positive and negative chemotaxis and the transformation of negative into positive chemotaxis by a process of adaptation. Similar observations may be made in human pathology; thus the tubercle bacillus is not positively chemotactic to pus cells (polymorphonuclear leucocytes), the colon bacillus is. (*v.* p. 219, Taxis.)

## Reaction to Injury Among Metazoa.

In the metazoa the cells are differentiated into three layers, an outer ectoderm, an inner endoderm, and a middle mesoderm. In the lowest metazoa (*e. g. Astropecten*) the mesoderm is composed largely of wandering ameboid cells. In these organisms, possessing no vascular nor nervous system, the reaction to injury is chiefly confined to the wandering cells which englobe and digest or expel foreign bodies which have penetrated the ectoderm of the animal. Among these lower metazoa also are seen some of the best examples of a remarkable power of regeneration exhibited by injured cells.

Among the higher metazoa, as man, the cellular reaction to injury is best seen in non-vascular regions such as the cornea. The reaction in the cornea may rarely be limited to swelling and multiplication of the corneal corpuscles, which replace those destroyed by irritants (as zinc chloride) without the intervention of wandering cells or the appearance of vascular changes. Usually, however, many wandering cells gather through the lymph spaces to the site of the injury, where they remove foreign matter and protect the regenerating corneal corpuscles. Even then the reaction to the injury may be limited to the cells and no vascular disturbance is present.

The phenomena of inflammation thus far considered include

therefore merely (1) the accumulation of wandering cells, leucocytes, and (2) the proliferation of fixed tissue cells. In all the more intense grades of inflammation in vertebrates these same cellular changes are present even to an increased extent, but their presence is usually obscured by more prominent vascular disturbances.

## Inflammatory Reaction in Vascular Tissues.

1. **Slight Vascular Disturbance. (Primary Union.)**—It is theoretically possible that reaction and repair after a clean incision of vascular tissue may be limited almost entirely to the fixed cells of the tissues, and some experimenters claim to have observed illustrations of this fact. In such cases the incision divides the cuticle, the connective tissues, and the small vessels. If the edges of such a wound be promptly apposed the hemorrhage is slight, the ends of the vessels are promptly closed by coagula, few tissue cells are destroyed and a slight fibrinous coagulum glues the surfaces together, so that at the end of an hour the wound appears closed and only a slight reddening about the incision indicates the moderate hyperemia of the blood-vessels. Into the coagulum the fixed connective tissue cells, irritated, send long processes, and new cells appear by multiplication of the old. The edges of the wound become more firmly united by these new cells and processes. The coagulum itself becomes condensed and fibrillated, presenting the characters of young connective tissue after the lapse of forty-eight hours. New capillaries are formed by the proliferation of the endothelial cells of adjoining vessels. Throughout the process little exudation from the vessels and few leucocytes are observed in sections of the tissues and the process is almost entirely limited to the fixed cells of the injured part.

The most successful cases of primary union of surgical wounds follow some such course of repair, but in the majority

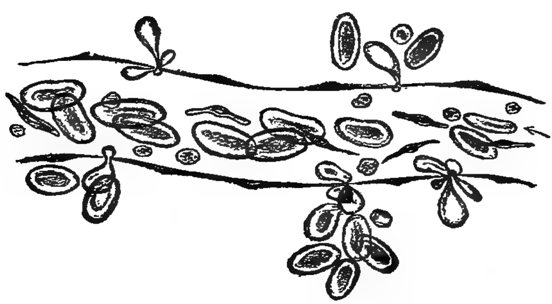
of instances, even of rapid primary union, sections through the line of incision will show some dead tissue-cells, a considerable number of leucocytes, and some exudation from the blood-vessels.

2. **Marked Vascular Reaction. (Secondary Union.)**

**Exudative Inflammation.** — The more extensive vascular changes which characterize inflammatory reaction have been most completely studied in clean wounds of the web of the frog's foot.

The injury causes, first, probably through the vasomotor mechanism, a dilation of the capillaries of the part, an increased flow of blood which continues for about an hour. Then follows a stage of slowing of the blood current and certain peculiar changes in the disposition of the blood cells and plasma.

FIG. 10.



DELAYED BLOOD STREAM, DIAPEDESIS. (*Stengel.*)
Capillary of frog's tongue. (Red cells nucleated in the frog.)

The leucocytes increase in number, they gather along the endothelial walls of the vessels, adhere to the swollen sticky endothelium, and by virtue largely of their ameboid properties they push their way through or between the endothelial cells out into the surrounding tissues, and especially to the surface of the wound. This process is called *emigration* of leucocytes.

Through the openings loosened by the passage of white cells, or more often through ruptures in the endothelial wall, aided by increased blood-pressure, red cells also pass out of the vessels, the process being called *diapedesis* of red cells. This process is more common in severe bacterial inflammations.

Exudation of blood-serum accompanies or rather precedes emigration and diapedesis. Through the swollen and more permeable endothelial cells the fluids of the blood, under increased pressure, are forced through the vessel walls to infiltrate the supporting tissues or appear on the surface of the wound. There is evidence also that the altered endothelial cells to some extent exert a true secretory action in discharging the blood-plasma. All these three processes tend to obscure the purely cellular reaction, which is nevertheless present and becomes apparent in the process of repair. After the vascular disturbance has somewhat subsided the proliferation of connective tissue cells, the budding of new capillaries from the adjoining small vessels, and the condensation of the new intracellular substance, may be seen in sections of wounds which are undergoing repair.

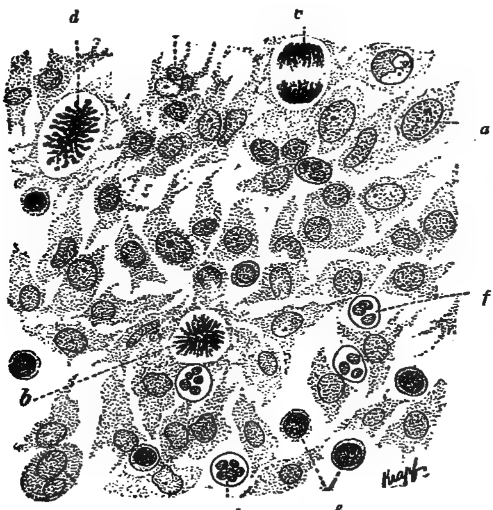
The above course of events is seen in surgical wounds which heal by secondary union in which the abundant exudate prevents immediate cohesion of the divided surfaces and healing begins only after the exudation has partly subsided, and usually progresses from the bottom of the wound outward. In some cases in which exudation rapidly subsides, as it should do in all aseptic surgical wounds, secondary cohesion of divided surfaces may occur, and healing follows after a variable period as in "primary union." If the cut surfaces are permanently held apart no cohesion can occur, and healing takes place by a slower process called *granulation*, which is best seen after suppurative inflammation.

3. **Intense Vascular Reaction. Suppurative Inflammation.**—When pyogenic microörganisms are carried into a wound and conditions are favorable for their growth, a more intense

grade of inflammation is excited, which is usually of the type called "suppurative." This process is best followed in tissues into which pure cultures of pyogenic cocci have been injected experimentally.

Within four hours after such injection the vessels in the neighborhood have been found to be gorged with blood, the blood current slowed, and leucocytes increased in number and partly adherent to the vessel walls. Such a condition is termed *acute congestion.*

FIG. 11.



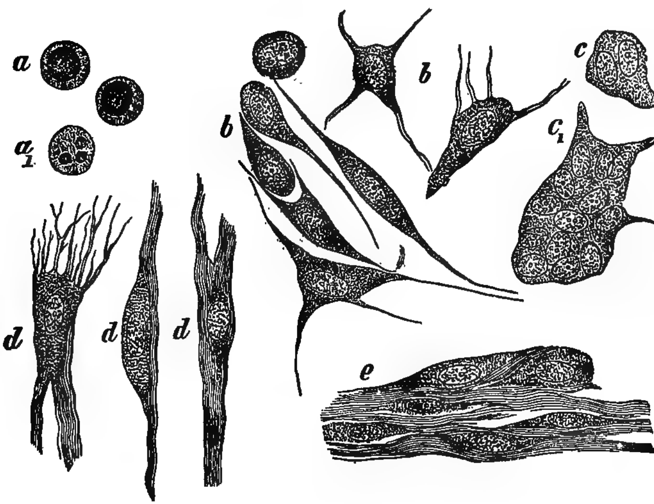

GRANULATION TISSUE. (*Coplin.*)

*a*, round cells before mitosis; *b*, monaster; *c*, diaster; *d*, formation of the skein; *e*, lymphocytes; *f*, polynuclear leucocytes.

After ten to twelve hours increasing numbers of leucocytes have emigrated from the vessels until the tissue is thickly infiltrated by these wandering cells lying in the distended lymph spaces. Diapedesis of red cells occurs in greater or less degree, and exudation of fluids from the blood is, in some cases, a prominent feature.

When such an inflammation occurs in a superficial surface, such as a mucous membrane, the emigrated leucocytes, extruded red cells, exuded serum and exfoliated lining cells form a copious purulent discharge from the surface, and do not damage the tissue by being retained under pressure. In deeper tissues, from which the exuded elements do not readily escape, their presence is more serious, and tends to obstruct the flow of

FIG. 12.



CELLS FROM GRANULATION TISSUE. (*Ziegler.*)

*a*, $a_1$, mono- and polynuclear leucocytes; *b*, forms of mononuclear new cells; *c*, $c_1$, bi- and polynuclear new cells; *d*, *e*, two stages of development of connective tissue from the new cells.

blood and to lead to degenerative changes in the tissue cells of the affected region. Nevertheless, in either situation the process may not go beyond the infiltration of the tissues with leucocytes and serum, and resolution follows without permanent damage to the tissue. A common example of this resolution is observed in the last stage of lobar pneumonia.

Healing of simple suppurative inflammations takes place after the subsidence of vascular disturbance, by the absorption of fluid exudate, and the liquefaction (largely by digestive ferments), and absorption of the cellular exudate.

**Healing by Granulation Tissue.**—When suppuration occurs in surgical wounds all attempt at cohesion of surfaces commonly fails and the wound is closed from the bottom up by a slow process called healing by granulation. Here, after partial subsidence of exudation, new capillaries develop from the cut surface, forming minute projecting tufts, supported by new connective-tissue cells, with a little intracellular substance and many wandering cells; this is known as granulation tissue. Such tissue has a granular surface, owing to the projecting tufts of vessels. By gradual increase in the quantity and density of the intracellular substance, disappearance of cells and obliteration of vessels, the tissue is transformed into dense connective tissue forming a scar or cicatrix. Epithelium finally covers the wound by gradual proliferation inward from the cut edges.

**Inflammatory Reaction with Local Death of Tissue. Necrotic Inflammation.** — When bacterial inflammation reaches a suppurative grade in a confined tissue it seldom resolves without causing some death of tissue and forming an abscess. The additional element of death of tissue throws this process into the class of necrotic inflammation.

The course of events in abscess formation may be carefully followed experimentally. The affected tissue becomes so thickly infiltrated with leucocytes and so much distended by exuded fluids that the vessels are compressed and occluded. All tissue cells thus cut off from nourishment promptly undergo acute necrosis and become more or less fluid. In some cases death and liquefaction of tissue occur apparently before there is sufficient exudate to compress the vessels, and the death of tissue is then referable principally to the necrotic action of bacterial toxines.

Sections through the region of an abscess disclose the presence of (1) a central cavity containing semi-fluid necrotic material composed of fragmented tissue cells, leucocytes, red cells, and usually an abundance of microörganisms. About this area there is (2) a zone of tissue in a state of intense purulent infiltration, while still further from the necrotic center (3) the tissues are in a state of intense congestion. Microörganisms in variable numbers may be found, partly in tissue spaces, partly englobed in tissue cells and leucocytes, in all parts of the abscess-wall, even to the edges of the congested area.

Healing of an abscess progresses slowly and is greatly facilitated by evacuation of the contents of the cavity and approximation of its walls. The vascular disturbance may then rapidly subside, exudation decreases, proliferation of connective-tissue cells and blood-vessels begins, and healing progresses as after simple suppurative inflammation, with the development of granulation tissue. A form of secondary cohesion of the abscess walls may occur which greatly diminishes the space to be filled by granulation tissue. All dead tissue is replaced, not in its original type, but invariably by granulation tissue and its final product, cicatricial tissue.

When the abscess is not evacuated healing is much slower. While considerable amounts of necrotic material may be removed by absorption and its remaining bulk reduced by desiccation, large abscesses often leave some necrotic matter which becomes surrounded by a fibrous wall and encysted. When the abscess is evacuated, but the walls are held apart, suppuration continues, the walls become lined by granulation tissue, which, being highly inflamed and discharging considerable pus, is sometimes called a *pyogenic membrane.*

## Inflammatory Reaction with Diffuse Death of Tissue.

**Diphtheritic Inflammation.**—Some intense chemical irritants and some bacteria, notably the bacillus of diphtheria,

when acting upon mucous membranes, excite an intense grade of inflammation characterized by considerable fibrinous and purulent exudation, and rapid death of superficial tissues. The coagulated fibrin entangles the elements of necrotic tissue, and tends to form a false membrane adherent to the surface of the inflamed part, whence the term pseudo-membranous inflammation is often applied to the process. Some forms of spreading suppurative inflammation of deeper parts cause rapid death of considerable areas of tissue, and much fibrinous exudate, and some writers apply the term diphtheritic inflammation to this process also. An example of this is the so-called diphtheritic erysipelas. Healing, if it occurs, follows the same course as in simple necrotic inflammation.

**Gangrenous Inflammation.**—In some forms of virulent and specific bacterial infection, but also as a result of cold, heat, pressure (bed-sores), ergot poisoning, and disease of the nervous system (syringomyelia), necrosis of tissue occurs rapidly and affects large areas. This type of inflammation is called gangrenous and the process gangrene. The necrosis is here the result of the ferment action of bacterial toxins or of compression of blood-vessels with anemia, or of the peculiar effects of heat, cold, etc. The dead tissues remain for a time attached to the living, but may be eventually thrown off as a slough or sphacelus by the exudation of leucocytes and serum along a line of demarcation. When the tissues remain moist from the presence of much inflammatory exudate the term moist gangrene is applied. Often there is little exudation, and the evaporation of fluids leaves the dead part comparatively dry (dry gangrene, mummification). Most bacterial infections induce moist gangrene. Senile gangrene, due to disease and occlusion of peripheral arteries, and most other non-bacterial varieties tend toward desiccation and dry gangrene. Some specific bacteria which often excite gangrenous inflammation are active gas-formers, and the resulting sphacelus contains many gas-

bubbles and is emphysematous. Among these are bac. aërogenes capsulatus and other putrefactive species.

When simple suppurative inflammation attacks the periosteum of long bones, conditions are peculiarly favorable for the occlusion of the nutrient artery supplying the shaft of the bone. When these vessels become occluded large portions of the shaft become necrotic and by reactive inflammation the dead mass is slowly extruded as a sequestrum.

## Invasion of the Blood Stream by Bacteria.

**Septicemia, Bacteremia.**—In all the bacterial inflammations thus far considered, the bacteria are confined more or less completely to the site of the local inflammation and few reach the general circulation. In some virulent infections in susceptible individuals, bacteria reach the general circulation and are to be found nearly constantly in cultures of the blood. This condition is called *septicemia.*

There is considerable latitude in the present application of the term septicemia. Some authors apply it indiscriminately to any condition in which there are symptoms of grave constitutional disturbance from absorption of toxins from a local inflammatory focus even when no bacteria can be found in the blood. This usage robs the term of special significance, since there is more or less absorption of toxins in all inflammatory processes. It is better to limit the term to those conditions in which bacteria may be found in the blood, the best example of which is found in general infection of the bloood by the *streptococcus pyogenes.* It remains true, however, that bacteria may be discharged into the blood from inflammatory foci at intervals, but if promptly removed by leucocytes and endothelial cells they cannot be demonstrated in the blood by cultures.

If the trend of usage should limit the term septicemia, as present indications seem to contraindicate, to that somewhat characteristic set of clinical symptoms which is associated with

profound intoxication by bacterial products, then the invasion of the blood stream by the bacteria themselves may be designated as bacteremia. At present clinicians constantly use the term septicemia to imply that there is invasion of the blood stream by bacteria, and the latter unequivocal term is, for this and other reasons, comparatively unrecognized.

In some cases of bacterial invasion of the blood the microorganisms are carried by the blood current to distant organs in which they lodge and give rise to local metastatic abscesses. Such a condition is termed *pyemia.* In cases of pyemia, cultures from the blood are usually negative till shortly before death.

In some cases there are symptoms of profound intoxication by bacteria and their products, as well as the development of metastatic abscesses and the condition is sometimes termed *septico-pyemia.*

**Resume.**—It thus appears that the inflammatory process may consist in:

1. A reaction limited entirely to the fixed cells of the tissue, or

2. A cellular reaction plus congestion of the vessels, or

3. Cellular reaction with congestion, to which is added exudation of blood cells and serum, or

4. Cellular reaction may be delayed and the exudation may be prominent and consist largely of leucocytes (suppurative inflammation), or

5. To the suppurative process may be added death of tissue and abscess formation (necrotic inflammation), or

6. Necrosis of tissue may be prominent from the first (diphtheritic inflammation), or

7. Rapid necrosis, with putrefaction, involving large areas of tissue may be the chief feature (gangrenous inflammation), or

8. Bacteria may temporarily or permanently invade the blood stream (septicemia, bacteremia).

# THE SEPARATE FACTORS IN EXUDATIVE INFLAMMATION.

We have thus far indicated the phenomena which occur in the different grades of acute inflammation. It is necessary to consider more in detail some of the processes concerned.

## The Vascular Changes.

After the initial acceleration of the blood current the slowing of the local circulation may progress until there is little or no movement of the blood, and a condition of partial or complete stasis is established. This is often followed by coagulation of the blood in the vessel, which thus becomes thrombosed. If the thrombosis occurs in large or medium sized vessels a portion of the thrombus may be dislodged and, reaching the blood current, may be carried to distant organs till it lodges in a smaller vessel. This process is called embolism, and the lodging mass an embolus. Emboli containing bacteria are probably the means of origin of many metastatic abscesses in pyemia.

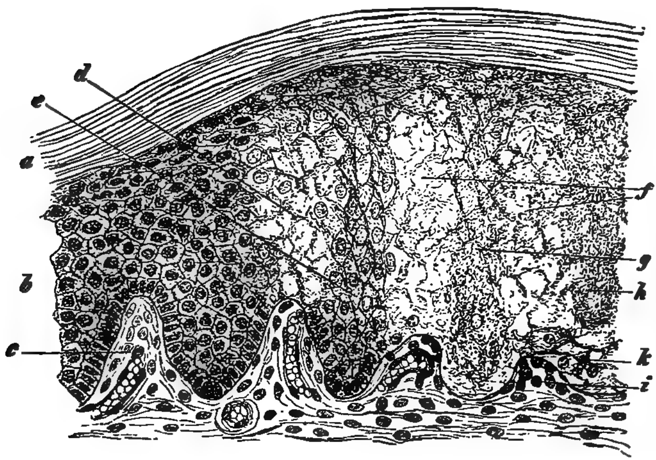
**Infarction.**—Areas of tissue cut off from their blood supply by embolism undergo a series of changes, tending toward necrosis. This process is called infarction and the affected area an infarct. When blood from collateral vessels makes its way by reflux into the infarcted region, this area becomes engorged with blood by the backward flow, and since the natural forces of circulation are cut off, the blood coagulates in the infarct. This process is called red infarction. In certain tissues collateral circulation is absent or imperfect (brain), no backward flow is established, the infarcted area remains bloodless and light-colored, and the process is called white infarction.

## The Fluid Exudate.

Another important series of vascular changes is largely dependent upon stasis in vessels in inflamed tissues. (1) Owing principally to lack of nutrition, the endothelial cells become

swollen and the spaces between them become wider, a condition which favors the exit not only of blood cells but also of blood-serum. Other factors favoring the exudation of serum are: (2) the increased blood-pressure in the distended vessels, (3) nutritive changes in the vessel wall, (4) alteration in the composition of the blood, (5) and changes in osmotic tension of

FIG. 13.




SECTION OF A VESICLE FROM BURN. (*Ziegler.*)

*a,* horny layer; *b,* rete Malpighi; *c,* normal papilla; *d,* hydropic cells of the rete, the nuclei still visible in places; *e,* interpapillary epithelia; below normal, above drawn out and swollen; *f,* cells entirely fluid; *g,* interpapillary epithelia, swollen, nuclei lost, loosened from the cutis; *h,* more complete destruction of cells; *i,* papilla, depressed and infiltrated with round cells; *k,* fibrin.

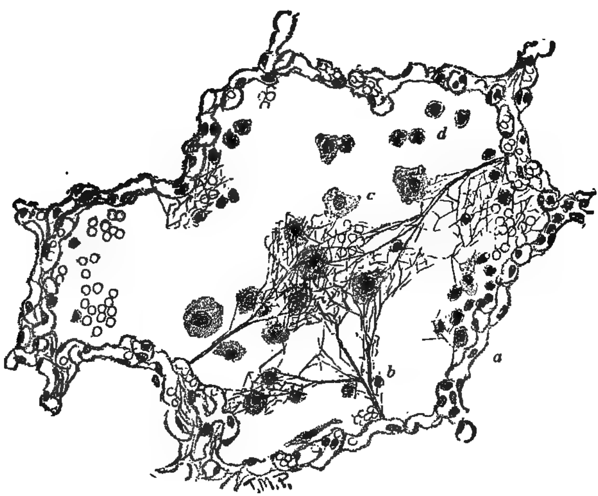
the intracellular fluids, while it is probable (6) that the irritated endothelium exerts a secretory action in the exudative process. Owing to different combinations of these factors the quality of the exudate varies widely.

When increased blood-pressure alone is present, as in cases of chronic endocarditis, the discharged fluid is called a trans-

udate and contains only a small proportion of the more easily diffusible albumin of the blood, serum-albumin.

When a true inflammatory process affects a connective-tissue or serous membrane, the exudate usually shows a higher proportion of albumins and a larger ratio of the less diffusible blood-albumin, serum-globulin, of which the presence indicates a more serious alteration in the vessel wall. Tissues infiltrated

FIG. 14.




EXUDATIVE INFLAMMATION IN THE LUNG. (*Delafield and Prudden.*)

*a*, alveolar wall; *b*, fibrin, entangling *c*, epithelia; *d*, pus cells.

by these fluid exudates are said to be edematous, or in a state of edema. Some forms of inflammation are characterized by the exudate of much fibrinogen, which soon coagulates, yielding a fibrinous deposit. In suppurative inflammation the exudate is composed of variable quantities of serum-albumin, globulin, fibrin and leucocytes. While albumin, globulin, and, in most

cases, fibrin, are usually completely absorbed in the healing process, the presence of many leucocytes in the interstices of a tissue is commonly followed by a more or less permanent deposit of mucin, and recovery of function is slow or incomplete. It is for this reason that a purulent infiltration has a more serious prognosis than a simple serous process.

## The Cellular Exudate.

(*a*) **Red Cells.**—The diapedesis of red blood cells is a prominent feature in some exudative inflammations. Their exit results from a loss of continuity of the vessel wall and from increased blood-pressure. Such exudates are blood-stained or bloody, and are described as sanguinolent or sero-sanguinolent according to the proportion of serum in the exudates. Bloody exudates usually indicate an intense form of bacterial infection, and the loss of blood is most abundant in the early stages of the process. Vascular tissues most often yield hemorrhagic exudates and some pathogenic bacteria have a special tendency to excite hemorrhage. Among these may be mentioned bac. coli communis, bac. tuberculosis.

**Hemorrhagic diathesis** is a term applied to an obscure constitutional predisposition toward hemorrhages, which here occur from slight traumatism or ordinary bacterial inflammations.

(*b*) **The Leucocytes in Inflammation. Leucocytosis.** The importance of leucocytes in inflammation has been clearly shown in the lower metazoa, in their behavior toward foreign bodies, which they englobe and digest or excrete. Although several varieties of new cells are found in inflamed tissues, the polynuclear neutrophile leucocytes are the most important variety, and it is an increase of this variety of cell which is usually indicated by the term leucocytosis.

In nearly all forms of exudative inflammation, especially in the suppurative type of bacterial origin, the leucocytes have an

important part to fulfill. In the early stages of the process the congested vessels are usually found to contain an excess of white cells, which it can be positively stated are attracted to the locality by the presence of bacteria and their products. This attractive force has been called, as stated, positive chemotaxis. Negative chemotaxis or a repelling force of bacteria upon leucocytes probably exists, but it is difficult to find any clear illustration of it. So active is this attractive force that the leucocytes will sometimes overcome considerable obstacles in order to reach the bacteria.

It might be supposed that the mechanical sifting of the cohesive leucocytes by the swollen endothelium may explain much of the local afflux of leucocytes, but it has been shown that the attractive force is exerted not merely in the inflamed focus but at a distance. Moreover, all the local changes in the blood-vessels may exist in some forms of inflammation without any local afflux of leucocytes. This has been observed in diphtheria in susceptible animals. Further, in most bacterial infections the leucocytes are increased in number not only around the inflamed tissue but throughout the general circulation as well, and in their sites of origin, the lymphoid tissues, pronounced evidence of increased formation of leucocytes has been found to accompany distant suppurative inflammations. We have, therefore, to distinguish—(1) a local and (2) a general intravascular increase of leucocytes, or leucocytosis.

**Significance of Leucocytosis.**—A long series of experiments has shown that the leucocytes are one of the important means of defense of the animal organism against bacterial invasion. (See Immunity, p. 238.)

If sections are made of tissues one hour after the subcutaneous injection in a rabbit of *bac. pyocyaneus,* the area surrounding the bacteria is found to be anemic, while the leucocytes are present in scanty numbers, having been apparently repelled or at least not attracted by the bacteria. This period corresponds to a stage of negative chemotaxis which occurs at the

beginning of most infectious disease and lasts a variable time, continuing until death in some virulent infections in susceptible animals and persisting only a few minutes or hours in milder infections or in refractory subjects.

If the sections are made several hours after the injection, the leucocytes are found to have gathered in large numbers at the site of the inoculation. Many white cells are found to have been destroyed by the bacteria and their products, but others are seen to have englobed the bacilli which may be found in various stages of degeneration. Under favorable conditions the leucocytes succeed in englobing and destroying all the bacteria, after which healing occurs as with aseptic wounds. The power to englobe and destroy bacteria is called *phagocytosis.*

There are great variations in the phagocytic power exhibited by leucocytes of different animals toward pathogenic bacteria, and this power is capable of being greatly increased by artificial immunization of the animal.

It appears to be a general rule that bacterial infections which pursue a favorable course are attended by marked local afflux of leucocytes which limit the growth of the microörganisms, while in unfavorable cases there is little or no leucocytosis, and the bacteria spread rapidly through the tissues causing the death of the animal. A practical illustration of this rule is seen in the well-known favorable significance of laudable pus, of which the yellowish color indicates a large proportion of leucocytes. In spreading necrotic inflammations, on the other hand, a thin sanious pus is commonly discharged which contains comparatively few leucocytes. Exceptions to the above rule are found with the *bacillus of tuberculosis* and less completely with the *bacillus typhosus,* which have little or no tendency to attract leucocytes or at least affect only one of the less numerous of the varieties of white blood-cells, the mononuclear.

Further support of the importance of phagocytic properties of leucocytes in inflammation is found in the marked bacteri-

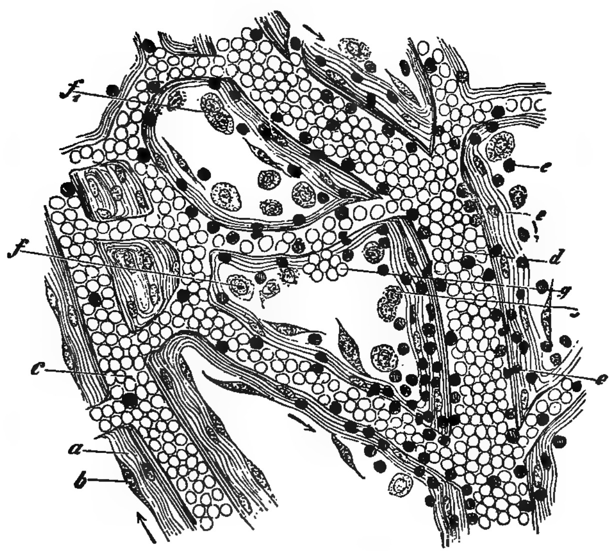
cidal action of purulent fluids in the test-tube. While many body-fluids, including blood-serum, exhibit considerable power in inhibiting the growth of bacteria in the test-tube, the most actively bactericidal animal fluid yet discovered was obtained from a purulent exudate into the pleural cavity excited by an aseptic irritant.

Before leaving the subject of phagocytosis it is necessary to emphasize the fact that the leucocytes are not the only elements in the body which exert bactericidal and phagocytic properties in inflammation. The blood-serum, as has been said, lymph, and mucus, exhibit varying degrees of bactericidal activity while endothelial, epithelial, visceral, and connective-tissue cells all exhibit more or less phagocytic power. (Phenomenon of Pfeiffer.) Although there has been much conflicting evidence, it may safely be said that the leucocytes are important agents in limiting bacterial infections, while essential aid in the function is furnished by the tissue cells and by tissue fluids. Local leucocytosis, therefore, indicates the effort to limit the spread of bacterial infection, while the intravascular leucocytosis measures the same effort to furnish leucocytes at the site of infection, and to rid the blood and system of absorbed bacterial products.

**Eosinophile Cells in Inflammation.**—Some forms of exudative inflammation are attended by a local increase in the number of eosinophile leucocytes. These cells are actively ameboid and emigrate from the vessels as do the neutrophile leucocytes. Eosinophile leucocytes are susceptible to chemotactic influences, as are neutrophile, but the chemical substances exerting the influence are peculiar. Ordinary excitants of inflammation have no attraction for eosinophile cells, but in many subacute or chronic inflammations, especially in the skin (*pemphigus*) or mucous membranes (*chronic bronchitis*) there may be a rich local eosinophile leucocytosis. A marked increase of these cells in the general circulation may accompany this local afflux, as these cells are derived from the bone-marrow, and they multiply to some extent after lodgment in the inflamed focus.

**Lymphocytes.**—In some forms of inflammation, especially of the subacute or chronic type, many lymphocytes gather at the inflammatory focus. Since these cells are not lacking in ameboid property they may respond to chemotactic influences, and their local afflux may also be assisted by purely mechanical causes. It is a rule that those inflammations which exhibit a

FIG. 15.




INFLAMED MESENTERY. (*Ziegler.*)

*a*, connective tissue, covered by *b*, normal epithelium; *c*, small artery; *d*, vein, leucocytes clinging to wall; *e*, leucocytes in emigration; *f*, $f_1$, desquamated epithelia; *g*, red cells after diapedesis.

special tendency to affect the lymphatic system and to spread through lymph-vessels induce lesions in which many lymphocytes are found. The classic instance of this is tuberculosis.

**Plasma Cells.**—In subacute and chronic inflammations some of the new mononuclear cells are larger than the lymphocytes,

possess a well-defined layer of homogeneous basophile protoplasm, and a single compact and usually eccentric nucleus. These cells have been termed plasma cells, and much has been written on their relation to forming connective tissue. Their origin and significance are uncertain, but they are distinguishable from large lymphocytes by special stains.

## The Changes in Fixed Tissue Cells in Exudative Inflammation.

As already stated, the initial injury which leads to inflammation always first affects the cells of a tissue, causing some degree of degeneration. Some cells coming into immediate contact with the injurious agent are at once rendered necrotic, and the earlier stages of degeneration are better studied in regions subjected to less violent action. The cells of the renal tubules furnish illustrations of well-defined stages of cellular degeneration. An earlier stage of degeneration is seen in the chromatolysis which ganglion cells suffer under some injurious influences.

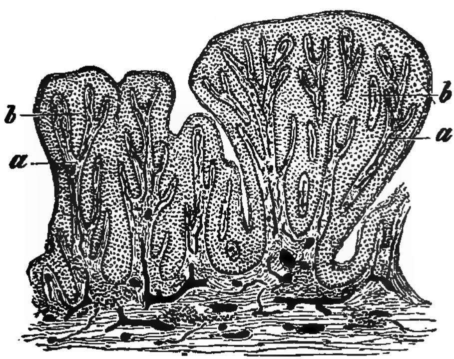
## Regenerative Changes in Cells in Inflammation.

We have thus far considered only the degenerative inflammatory changes in cells, but inflammation commonly induces some important regenerative processes in the affected cells. Remarkable examples of reproductive activity of injured cells are seen in some low animals (thus hydra develops an entire set of tentacles about points of incision on its stem). Among vertebrates whose tissues are more highly differentiated acute inflammation causes more degeneration than regeneration, especially in the parts most intensely inflamed, but in surrounding areas marked evidence of proliferation of cells is usually observed, and it has already been mentioned that the healing process is largely the result of the regenerative activity of endothelial and connective-tissue cells.

In fibrino-purulent inflammations of serous membranes striking illustrations are seen of the proliferating tendency of inflamed endothelium.

Subacute inflammation of serous membranes may consist almost entirely of congestion of vessels and proliferation of large numbers of lining cells and fibroblasts, but with little or no exudation. This process is therefore sometimes called cellular inflammation. The product of such an inflammation is at first a tissue composed largely of the new cells with a little intracellular substance and some new blood-vessels. Later the tissue shows many of the characters of fibrous connective tissue.

FIG. 16.




CONDYLOMA ACUMINATUM. (*Ziegler.*)

*a*, enlarged branching papillæ; *b*, epidermis, reaching to the bases of the hypertrophied papillæ. An example of inflammatory new growth.

Pure examples of the inflammatory growth of new connective tissue are seen in some subacute inflammations of the kidney, where the chief alteration observed is an increase in the quantity of the supporting stroma of the organ. This new tissue is composed of new branching fibroblasts (connective-tissue cells) and moist finely fibrillated intracellular substance.

In tuberculous and syphilitic inflammations the chief result may be a proliferation of fibroblasts and endothelial cells but usually there is a moderate exudation of leucocytes and serum, producing a peculiar type of tissue called tubercle tissue; it consists of granular intracellular substance, large epithelioid fibroblasts, mononuclear and polynuclear leucocytes, and giant cells. The giant cells are a characteristic feature of tubercle tissue, and are formed usually by the fusion of several cell-bodies with multiplication of nuclei. They are occasionally seen in exudative inflammation from other causes. In some tuberculous or syphilitic foci, there gather large numbers of mononuclear leucocytes or lymphocytes, which form a characteristic type of tuberculous nodule, called the lymphoid tubercle.

Those forms of inflammation which result chiefly in the formation of new tissue are called productive inflammations. The two main types of inflammatory reaction may now be said to be (1) the exudative and (2) the productive. A great many examples exist of mixed exudative and productive processes. While the final product of productive inflammation is nearly always fibrous tissue, it by no means follows that all this fibrous tissue is to be classed as true connective tissue. True connective tissue probably arises only from preëxisting connective-tissue cells, while the fibrous areas which result from proliferating endothelium, epithelium, and leucocytes have a somewhat different significance. Nevertheless, it is practically impossible to determine the true origin of all the fibrous products of chronic inflammation, and equally difficult to follow the fate of many exuded leucocytes which are nearly constant in inflammatory new connective tissue. The burden of proof lies with those who claim that leucocytes may be transformed into fibroblasts, which has not yet been demonstrated. Endothelium may undoubtedly produce a tissue which closely resembles connective tissue, but of leucocytes it can only be said that most of them disappear or retain the character of wandering cells, and that mononuclear leucocytes sometimes become

passively incorporated in new connective tissue, without contributing essentially to its formation.

## Inflammatory and Non-Inflammatory Fibrous Hyperplasia.

While many deposits of new fibrous tissue can with certainty be referred to an inflammatory process, fibrous overgrowth often occurs under conditions which render an inflammatory origin improbable. Thus, the dense connective tissue found in old cases of nephritis or cirrhosis of the liver is clearly the result of a previous productive inflammation. Similarly the areas of connective tissue which replace an infarct of the spleen are plainly referable to a reactive inflammation excited by the necrotic tissue of the infarct.

On the other hand the extensive overgrowth which occurs in the female breast after the menopause is certainly not referable to inflammation, nor is it of neoplastic origin. The fibrosis which occurs in the lateral tracts of the spinal cord in cases of cerebral apoplexy has none of the distinct antecedents of inflammation but merely follows the atrophy of the medullated fibers, whose cells of origin have been destroyed by a cerebral hemorrhage.

It is therefore necessary to distinguish between inflammatory and non-inflammatory fibrous hyperplasia. The majority of non-inflammatory hyperplasias are believed by many to be referable to disordered nutrition of the part, the relatively low type of fibrous tissue persisting and even increasing in nutritive conditions which are unsuited to cells of higher function. Thus replacement fibrosis occurs in the heart in proportion to atrophy of the muscle cells and the simplest form of this is seen as a senile change; is called fibrous myocarditis, but it is not strictly an inflammation or the result of it and hence does not deserve the termination -itis. Similar fibrosis may occur in nearly all tissues.

Marked grades of inflammatory hyperplasia are seen in other tissues. The lymph-nodes in the neighborhood of an infected wound are often found much enlarged, partly from hyperemia, or exudation, but principally from a marked increase in the number of lymphoid cells, which are actively stimulated to new production by the irritant.

Subacute and chronic inflammations of mucous membranes, especially of the nasal and uterine mucosæ, often result in much increase both of the cells and the fibers of the stroma, and in the number, length and tortuosity of the glands. Some of the frequent.

FIG. 17.

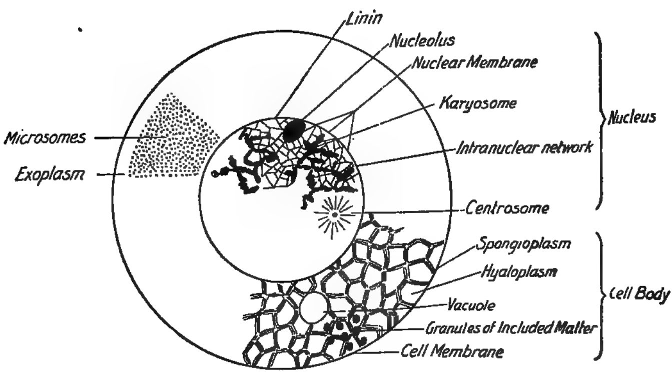



DIAGRAM OF THE PARTS OF A CELL. (*A. E. T.*)

inflammatory hyperplasias in mucous membranes reach almost to the grade of neoplastic growth.

**Cell Division.**—Part of the process of repair consists in cell reproduction. This occurs when an injured tissue is regenerated or its place taken by other tissue cells, regeneration being less common in higher animals than repair. Cells multiply in two ways, indirectly, by *karyokinesis, karyomitosis* or simply

*mitosis,* and directly by *amitosis;* the former is more frequent.

A cell is a microscopic mass of protoplasm provided with a nucleus and exhibiting function, and is the ultimate physical unit of plants and animals. Roughly the cell may be divided into cell body or protoplasm, nucleus, enveloping membranes and certain other structures, as appears from the diagram:

SUMMARY OF THE PARTS OF A COMPLETE TYPICAL ANIMAL CELL.

| | | | |
|---|---|---|---|
| Complete typieal cell | Cell body or Cytoplasm or Protoplasm | made up of | 1 Spongioplasm or cytoreticulum<br>2 Hyaloplasm or cytolymph<br>3 Microsomes<br>4 Cell membrane enclosing all |
| | Nucleus or Karyoplasm | made up of | 1 Intranuclear reticulum { chro-matin, linin }<br>2 Karyolymph<br>3 Karyosomes or pseudo-nuclei<br>4 Nucleolus<br>5 Centrosome<br>6 Nuclear membrane enclosing al |

The cytoplasm is granular or homogeneous and consists of a meshwork of spongioplasm, called the cytoreticulum, enclosing in its spaces the fluid hyaloplasm, the proportion between these two elements varying from time to time and in different cells; as a rule the younger cells have relatively more hyaloplasm and less spongioplasm and the older the converse of this. Imbedded in the cytoplasm are many fine granules called microsomes, which are seldom uniformly disturbed, but are less numerous about the periphery, exoplasm, and often gathered in certain sections of the cytoplasm; if very numerous these microsomes give the cell body a dark look. Fragments of foreign matter and empty spaces or vacuoles are also common appearances in the cell body.

The nucleus is the focus and source of the cell's activity; usually it lies well within the cell body but occasionally it stands out like the cornea on the sclerotic. It bears a certain relation to the size of the cell but may occupy nearly the whole of the

cell membrane's capacity (lymphocyte). In form it is spherical, ovoid or irregular, and may be single or many. The only cells normally without nuclei in the human body are those of the epidermis (outer layer), of the terminal respiratory passages and the red blood cells. The resting nucleus shows a nuclear membrane of two layers, the inner staining and called the chromatic, the outer taking no stains and called the achromatic layer. This encloses the karyoplasm, which is made up of a double network and holds lymph in the meshes, called karyolymph. The network shows delicate fibers which do not take stains, called linin, and which support the heavier and nodular recticulum of chromatin, which is the element with special affinity for nuclear stains; in the latter certain nodal points of thickened material are called karyosomes and simulate nuclei; the chromatin may be threads, rods or granules. The nucleolus, or true plasmasome, is a small body of unknown function which takes the nuclear stains with avidity, lying free in the cavity of the nuclear membrane or attached by linin fibers; at the beginning of division it is extruded and disappears, to return at a later stage.

The centrosome is a small spherical body which acts as the directing force in the arrangement of the chromatin bundles during division; it is then surrounded by a halo of rays which together make the attraction sphere or archosome.

The nuclear and cell membranes are comparatively unimportant envelops for the elements of each.

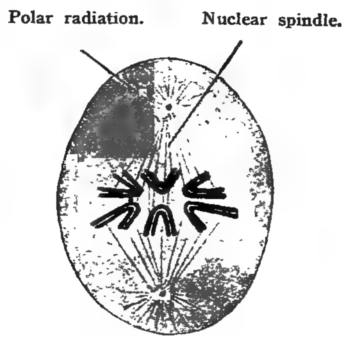
**Function.**—Broadly grouped, all the activities of cells fall under one of the following heads:

1. Movement, which may be protoplasmic, ameboid, or ciliary; that is, there may be currents of flow in the cytoplasm, or the cell may put out large processes, pseudopods, or it may be provided with fine projecting hair-like processes which keep up a lashing motion.

2. Irritability, by which is meant the response to external stimulus, mechanical, thermic, photic, electric, chemic, positive or negative cyto-taxis.
3. Metabolism, consisting as elsewhere of anabolism or true nutrition and catabolism or waste and excretion.
4. Reproduction, by mitosis, that is indirectly, or by amitosis, directly.

**Cell Kinesis.**—In the indirect form of reproduction the various parts of the cell exhibit a number of complicated movements

FIG. 18.




SCHEME OF THE MOTHER STAR. (*Stohr.*)

Two centrosomes, equatorial plates of divided V's, spindle and attraction spheres, the whole surrounded by cytoplasm at the beginning of the metaphase.

and divisions, the energy therefor being doubtless derived from chemical energy set free in the course of the cell's metabolism and stored toward the end of the resting stage. It is usual to describe the process in four stages, each called a phase, the entire series taking from 30 minutes, in man, to five hours, in amphibia:

1. Prophase. The nucleus prepares for the coming division, it enlarges; the centrosome passes out

into the cytoplasm and divides, the first actual division in the process. rarely it divides before extrusion; the daughter centrosomes move then to opposite poles of the nucleus, each surrounded by its rayed attraction sphere or archosome; the rays passing from one centrosome to the other arranged as a spindle of threads (linin) in equidistant meridians; along these the chromatin rods are directed. The entire figure of centrosomes, rays about each, and

FIG. 19.

SCHEME OF METAPHASE. (*Stohr.*)

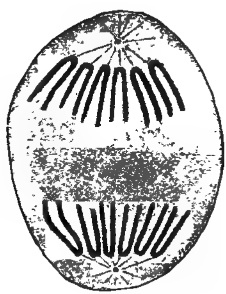
Two centrosomes, spindle, and dividing chromatin V's, surrounded by cytoplasm.

certain rays common to both making the spindle, closely resembles the lines of magnetic force along which particles of iron arrange themselves on a paper when the two poles of a magnet approach it from below. The chromatin threads become less numerous, shorter and thicker, arranged in a tangle or wreath. The nucleolus and nuclear membrane disappear. The chromatin is now arranged in short rods, each

bent in the middle to less than a right angle, forming a V; varying in different animals from 2 to 36, for man 16; the V's collect at the equatorial plane of the spindle, the angles turned in to the main axis of the spindle, thus making the equatorial plate or monaster.

2. Metaphase. The V's split along their length so that a double equatorial plate is formed and each group of halves begins to draw toward its corresponding pole or centrosome, angle first. This is the second actual division of cell elements.

FIG. 20.



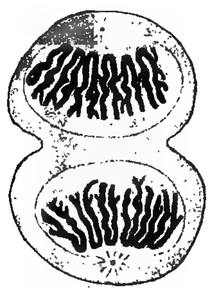
SCHEME OF THE EARLY ANAPHASE. (*Stohr.*)
Divisions of chromatin complete, the half V's collected at each pole.

3. Anaphase The divided V's are collected about each centrosome, forming the diaster, and an indentation appears in the cytoplasm at the level of the equatorial plane. This is the third division.
4. Telophase. This construction moves inward along the mid-transverse plane and completes the division of the cell; each half containing exactly half of the chromatin half-V's, one of the daughter centrosomes and half the cytoplasm.

In each part a nucleolus and a nuclear membrane appear and the resting stage is again attained. The essential element in this process is the chromatin, and hence its rods and V's are regarded as the carriers of hereditary characters.

In amitosis, which in the human being is seen only in leucocytes, lymphocytes and the cells of some neoplasms, the nucleus simply constricts, its halves draw apart, and with this a con-

FIG. 21.



SCHEME OF THE EARLY TELOPHASE. (*Stohr.*)

Cytoplasm incompletely divided, centrosome in each nucleus, chromatin still disposed in V-shaped figures as it arrived in each, but beginning to branch into network, nuclear membrane forming.

striction appears in the cytoplasm; both nucleus and cytoplasm occasionally lengthen out to fine threads before completely dividing.

Abnormal examples of mitosis are found in which there are more than two centrosomes (called multipolar), or where the equatorial plate divides into more than one set of split V's, or the diaster may divide secondarily; and in others, perhaps under conditions of pressure and rapid division, the nuclei divide and redivide while the cell body remains undivided, only

enlarging to accommodate the numerous nuclei, and thus forming giant cells. Experimentally some of these abnormal forms may be reproduced by treating the dividing cells with various chemical solutions, which irritate or inhibit in some unexplained way, or by conditions which are mechanically unfavorable.

A form of abnormal direct division is known as nuclear fragmentation or karyorhexis.

The cells which may be found in various inflammations are the following:

| Name. | Nucleus. | Protoplasm. | Stain. |
|---|---|---|---|
| 1. Eosinophile, large or small | coarsely reticular, often bi-lobed | contains acidophile granules | eosin |
| 2. Epithelioid, also called clasmacyte in sheath of vessels. | large, vesicular | acidophile | eosin fuchsin. |
| 3. Fibroblast, fusiform or branched, | oval, vesicular | granular, usually basophile | hematoxylin. |
| 4. Giant cells | many, grouped in middle or along margin | may be coarsely granular | basophile. |
| 5. Leucocyte, large mononuclear | vesicular, lobed, or horse-shoe, coarsely reticular. | finely reticular | slightly basophile. |
| 6. Leucocyte, polynuclear, pus cell. | lobed or separate, two or more, coarsely reticular. | neutrophile granules. | slightly basophile. |
| 7. Lymphocyte, small round cell, common in lesions of syphilis and tuberculosis | compact, spherical | narrow rim about nucleus | basophile. |
| 8. Mast cell, irregular shapes. | usually single | basophile granules | polychrome and thionin blue. |
| 9. Plasma cell. | round, eccentric, stains irregularly. | denser along edge | methylene blue |
| 10. Pseudo-plasma cell, larger than 9. | may be eccentric | homogeneous | acidophile |

Young cells produced as above resemble the parent cell; a connective tissue or a cartilage cell would not divide into two epithelial cells. The life of all cells is limited and as they grow old there is a decrease in the volume of both nucleus and cell

body with irregularities in the chromatin; vacuoles may appear even in the nucleus. The growth of cells is rarely symmetrical; usually it follows two axes, a major and a minor, making elongated, cylindrical and flattened figures; pressure from surrounding cells doubtless is of great influence here, both direct and transmitted.

Cells are held together by products of their own metabolism (cement substance) which is often homogeneous but may take on a fibrillar structure; other products are held in the cell or removed for elimination.

## INFLUENCE OF THE NERVOUS SYSTEM UPON INFLAMMATION.

The nervous system has a prominent influence in controlling the vascular phenomena of inflammation, for if its influence is cut off the stage of exudative inflammation follows more rapidly than in a normally innervated part.

If the sympathetic nerve filaments passing to the rabbit's ear be divided, the vessels dilate, inflammatory changes when excited follow rapidly and healing is likewise more prompt. If, however, the spinal cord filaments be divided, the vessels contract under the influence of the sympathetic, and inflammatory changes follow traumatism more slowly, exudative phenomena are less marked, but stasis is more apt to occur in the vessels and gangrene more frequently follows upon injury. These interesting experiments illustrate the difference in the action of the two sets of nerves, but do not appear to have a wide practical application. The peripheral network of nerve filaments and ganglion cells immediately surrounding arterioles and capillaries appears to be purely sensory, and the effects of the inflammatory process resulting from its destruction have not been determined.

It is an important fact that inflammation in an area supplied by one portion of a nerve trunk may excite some inflammatory

disturbance in areas supplied by other portions of the same trunk.

Finally, cerebral nervous influences have undoubtedly alone induced inflammatory phenomena.

## CLASSIFICATION AND NOMENCLATURE OF INFLAMMATIONS.

Inflammations are classified according to the most marked feature of the inflammatory process, which varies with the structure and position of the tissue affected and with the nature and intensity of the irritant.

The termination -itis has been tacitly agreed upon to represent inflammation of the part whose name precedes it, as bronchitis, peritonitis. This termination is derived from the Greek feminine adjective ending in -ιτις, and some word for disease (νόσος) is understood. Certain inflammations do not carry this ending, as pneumonia for inflammation of the lungs, angina for inflammation in the tonsils and floor of the mouth, and phlegmon for subcutaneous inflammation. The prefix peri- indicates that the inflammation is in the immediate neighborhood of an organ, sometimes in its capsule, as periarteritis, perisplenitis, or is in a serous membrane, as pericarditis; the prefix endo- refers to inflammation of the lining of hollow organs, as endocarditis; para- locates the lesion in adjacent connective tissue, as parametritis. This usage is not always consistent.

### 1. Degeneration.

The inflammatory process may not go beyond degeneration, followed by regeneration of tissue cells, while vascular phenomena are almost entirely wanting.

Very mild chemical irritants or traumatism applied to cutaneous or mucous surfaces or affecting deeper tissues may cause only a certain grade of degeneration of tissue cells, which is promptly repaired without vascular disturbance. In the infec-

tious diseases all the internal viscera are exposed to the toxemia and the cells suffer some grade of degeneration. Since it is the cells or parenchyma of the viscus which especially suffer, the change in the viscera is commonly called parenchymatous degeneration.

The different infectious diseases show a tendency to affect special tissues and organs. In typhoid fever the muscles suffer; in diphtheria it is the peripheral nerve fibers; in yellow fever, the liver, and in scarlet fever the kidneys. The grade of degeneration depends upon the intensity of the irritant, the cells showing swelling, granular degeneration, fragmentation, or fatty changes. In the severer forms congestion and a little exudation from the vessels are frequently added to the cellular changes. The function of the organ suffers in a degree corresponding to the grade of degeneration. The cells may recover from the milder forms of degeneration, while necrotic and exfoliated cells are replaced by new ones of the same type.

## 2. Exudative Inflammation.

Exudative inflammation is marked chiefly by vascular changes and the presence of an exudate of serum, fibrin, pus, and blood. The character of the exudate varies greatly according to the intensity of the irritant and the structure of the tissue.

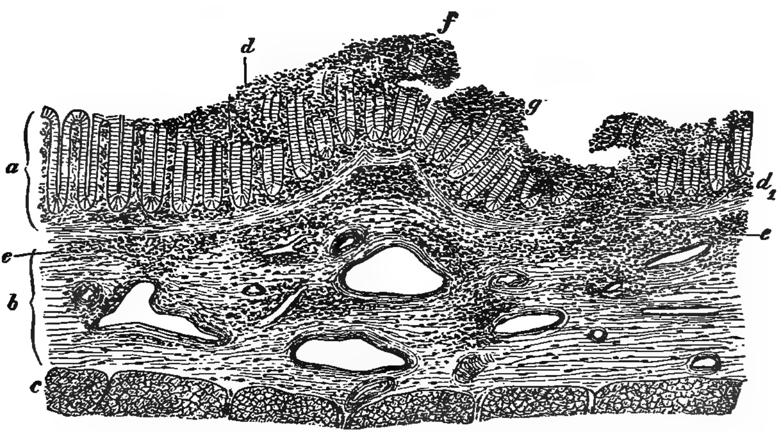
If the exudate consists largely of serum, the process is termed serous inflammation, if of fibrin it is called fibrinous inflammation, and if of pus, purulent inflammation, etc., with combinations of these types. These grades of inflammation vary principally with the nature of the irritant.

The effects of the inflammatory process depend upon the structure of the tissues.

(*a*) **In connective tissue** the intracellular substance may be swollen and infiltrated by the exudate. The vessels are congested and all the cells suffer more or less alteration. When the process subsides serum is readily absorbed by blood vessels

and lymphatics; fibrin is more slowly liquefied and absorbed. Many pus cells may be disintegrated and absorbed, but after an excessive exudate of pus, and much degeneration of cells, a more or less permanent deposit of mucin is apt to be left in the tissue. When an inflammatory process of any type affects the supporting connective tissue of a viscus it is called an interstitial inflammation.

FIG. 22.




DYSENTERY. SUPPURATION AND NECROSIS OF THE MUCOSA OF THE COLON. (*Ziegler.*)

*a*, mucosa; *b*, submucosa; *c*, muscularis; *d*, *d*, infiltration of the inter- and subglandular tissue, *e*, of the submucosa; *f*, upper glandular layer sloughing off; *g*, ulcer thus produced, its floor infiltrated with leucocytes.

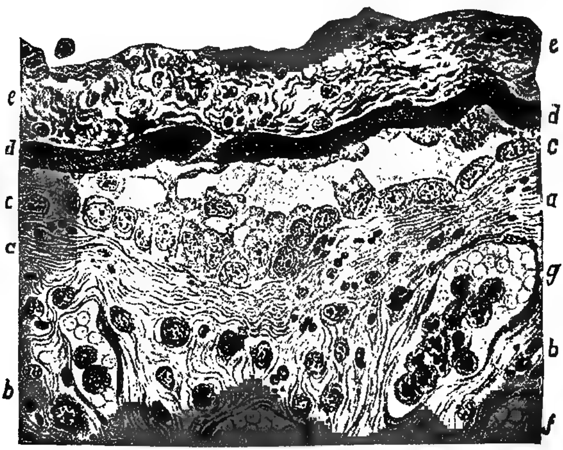
(*b*) **Mucous Membranes.**—Simple exudative inflammations are often limited to mucous membranes, and are then called catarrhal inflammations.

The changes affect (1) the stroma, which is composed of reticular connective tisue, supporting many lymphocytes, and richly supplied with lymph- and blood-vessels, and (2) the glandular layer, containing glands with epithelial lining.

The stroma suffers the usual changes of exudative inflammation in connective tissue, often varied by the multiplication of lymphocytes.

The glandular layer suffers from the exfoliation of epithelial cells, often leading to superficial erosions or ulcers, which are repaired later by the new growth of epithelial cells. The function of the glands is disturbed. At first the secretion of mucus

FIG. 23.




FIBRINOUS PLEURISY. (*Ziegler.*)

*a, b,* inflamed pleura; *c,* investing epithelia swollen and exfoliating; *d, e,* exudate of fibrin with serum and pus cells; *f, g,* blood-vessels, containing red cells and polynuclear leucocytes.

is inhibited (dry stage); later it is increased and often altered in quality, and at the same time the congestion of the vessels is to some extent relieved. This relation of increased secretion to congestion of a mucous membrane is of importance in therapeutics. The duration of the "dry stage" in catarrhal inflammation varies in different mucous membranes, and seems to bear some relation to the amount of lymphoid tissue in the membrane.

Rich fibrinous exudates sometimes form on mucous surfaces and adhere to them as a pseudo-membrane, but without the necrosis of cells which occurs in diphtheritic processes.

The term croupous inflammation is properly applied to one in which the exudate of fibrin is a prominent feature, but the diversity of usage which this term suffers renders its employment inadvisable.

(*c*) **Serous Membranes.**—In serous membranes the subserous connective tissue suffers as usual, but the exudate, whether serum, fibrin or pus, is usually poured out in large and often in enormous quantities. Thus a liter of highly albuminous serous fluid is often thrown off by the pleura in a few hours, a layer of fibrin 1 cm. in thickness may form in a few days, while empyema (purulent inflammation) frequently causes such a large exudate of pus that the lung is tightly compressed against the spine. A similar excess of exudate occurs in inflammations of joint cavities, meninges, etc.

(*d*) **Lymphoid Tissue.**—In the lymph nodes and spleen the supporting stroma suffers as usual in exudative inflammation, and there is commonly a pronounced multiplication of lymphocytes, especially about the lymph nodth. The framework of a lymphoid organ is a labyrinthine meshwork in which the strands of reticular tissue are lined by endothelial cells. One of the prominent effects of exudative inflammation here is the exfoliation of large numbers of edothelial cells, often without much exudation, and the process is therefore rightly called catarrhal inflammation. The term catarrhal calls attention especially to the exfoliation of lining cells.

(*e*) **Viscera.**—In the viscera, the stroma may become swollen, edematous, and infiltrated with leucocytes, and these exuded products, usually in small quantity, may be found between the epithelial parenchyma cells, and in the lumen of the alveoli. The cells suffer varying grades of degeneration; their function is interfered with or inhibited; and secreted products are often rendered pathological in character. When the stroma of a vis-

cus is exclusively affected, it is called interstitial inflammation. When the functioning cells are chiefly affected it is called parenchymatous inflammation, and when all parts of the viscus are involved it is called diffuse inflammation. These terms indicate the location but not the grade of inflammation.

### 3. Necrotic Inflammation.

Intense bacterial or chemical irritants often lead to exudative inflammation with death of considerable portions of tissue, hence the term necrotic inflammation is applied.

In connective tissue, when the exudate compresses blood-vessels and shuts off the blood supply, or when bacterial products exert an intense necrotic action, a portion of tissue dies and is partly liquefied, and an abscess is produced.

In mucous and serous membranes and on cutaneous surfaces the same factors lead to the death of a superficial area of tissue, which is readily thrown off as a slough, leaving an ulcer.

The superficial ulcers of catarrhal inflammation are healed by proliferation of epithelial cells, completely restoring the surface, but the deeper ulcers of necrotic inflammation affecting the stroma, are healed by granulation tissue and leave a cicatrix.

In the viscera, abscess, focal necrosis, and death of larger areas of stroma and cells result, which heal if at all by granulation tissue, leaving cicatrices. Isolated necrotic epithelium may be replaced by new cells of the same kind.

### 4. Diphtheritic Inflammation.

Diphtheritic inflammation is the term employed when the process is marked by widespread necrosis, either superficial and involving principally the epithelium, or deeper and extending through the mucosa or even through the submucosa. There is at the same time more or less fibrinous exudate entangling the necrotic elements and adhering firmly to the surface as a false membrane. This process is sometimes called pseudo-membran-

ous, and also, though improperly, croupous inflammation. Now diphtheritic inflammations may not form any false membrane whatever, and simple fibrinous exudates without necrosis may produce abundant pseudo-membrane, so that the three terms — diphtheritic, pseudo-membranous, and croupous — cannot be considered synonymous. It is better to avoid the use of the latter terms altogether, since they do not accurately indicate the grade or type of inflammatory process.

In connective tissues diphtheritic inflammation is not infrequently seen, but is seldom fully recognized, being often classed with spreading suppurative or with gangrenous processes. Here it is marked as usual by diffuse necrosis and liquefaction, or when fibrin is abundantly exuded, by necrosis and coagulation.

In mucous membranes diphtheritic inflammation produces widespread necrosis. The depth of the necrotic process varies. If it affects only the epithelium, superficial erosions are produced, usually with much exudate and fully repaired by proliferation of surrounding intact epithelium. If it attacks the stroma of the mucosa or submucosa true ulcers are formed, healed by granulation tissue and covered over by flat or cuboidal, but not by specialized epithelium.

If the exuded and necrotic elements are rapidly liquefied no false membrane is produced. This is the case in malignant diphtheria of the pharynx. Usually a membrane is formed, as described, by the coagulation of the necrotic tissue cells and exuded elements. Such false membranes are usually exfoliated by means of a reactive purulent inflammation in the underlying tissue.

In viscera it is usually difficult to recognize diphtheritic processes from simple necrotic or from gangrenous processes. In the kidney they frequently arise by ascending infection from diphtheritic cystitis.

**Types of Ulcers.**—Three types of ulcers have been described:

1. From death of lining epithelium only. Such ulcers or

erosions result both from catarrhal and from diphtheritic processes, and are usually of small dimensions.

2. From simple necrotic inflammation. Such ulcers involve varying depths of superficial tissues and are usually well circumscribed.

3. From diphtheritic processes. Such ulcers are of variable depth and are often of large dimensions.

Many descriptive terms are applied to ulcers, based upon their principal characters, which relate to their

Number and grouping.

Base and secretion.

Edges and vicinity.

## 5. Productive Inflammation.

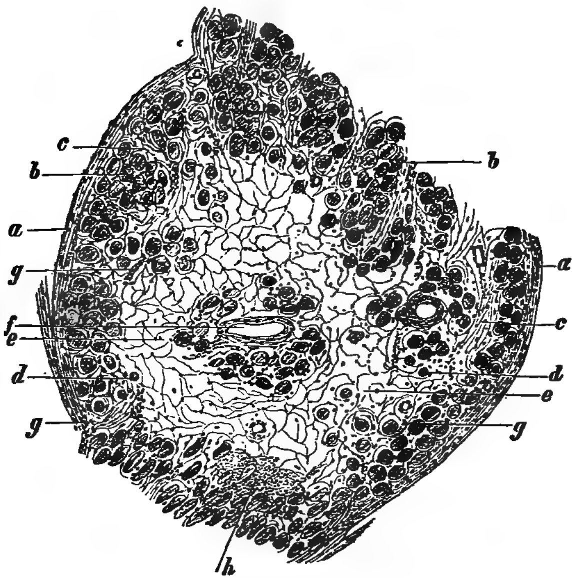
Productive inflammation is characterized by the development of new tissue. There may be no accompanying exudation whatever, in which case the process is called simple productive inflammation, or exudation may be added, in productive inflammation with exudation. The latter is much the commoner form.

### (*a*) Simple Acute Productive Inflammation (Cellular Inflammation).

Pure types of this process, though rarely encountered, are furnished chiefly by serous membranes, as the peritoneum, pleura, and meninges. The new tissue is composed of new cells formed from fibroblasts and endothelium, while the neighboring vessels are usually in a state of moderate congestion. Owing to the character of the new tissue produced and the absence of vascular changes this process is sometimes called cellular inflammation. Later the new tissue approaches the type of adult fibrous tissue, and causes a permanent alteration in the structure of the affected part. The development of a cellular inflammation requires a tissue composed of cells with active proliferating capacities, and an irritant of slow action and mod-

erate intensity. The purest examples have been furnished experimentally, from the application of mild caustics to the peritoneum. It is frequently seen in serous surfaces bounding areas

FIG. 24.




FIBROSIS IN CARDIAC PAPILLARY MUSCLE. (*Ziegler.*)

*a*, endocardium; *b*, normal muscle; *c*, fibrous hyperplasia, rich in cells; *d*, atrophic muscle; *e*, fibrous tissue with few nuclei and no muscle cells; *f*, a vein, with a few muscle cells about it; *g*, small blood-vessels; *h*, round-cell infiltration.

of more extensive exudative inflammation, as on the pleura in pneumonia, or on the peritoneal surface of the intestine near the ulcers of typhoid fever.

## (*b*) Productive Inflammation with Exudation.

Acute productive inflammation is usually accompanied by vascular changes and by exudation from the vessels. The exudate consists of serum, fibrin, or pus, as in simple exudative

inflammation. The new tissue is derived from fibroblasts which are at first numerous and are soon surrounded by delicate intracellular substance. It may contain many mononuclear leucocytes which at this time are indistinguishable from fibroblasts, and it may also be infiltrated with some polynuclear leucocytes. New capillaries are developed from neighboring vessels, but the new tissue is often imperfectly vascularized from the first and prone to various forms of degeneration or even necrosis. During recovery the exudate may be removed in the usual way, but the new tissue remains as a permanent alteration of the affected part. The final product is usually a dense fibrous tissue.

It is characteristic of productive inflammations with exudation that they are subacute rather than acute in their course, that their duration is protracted and that the acute stages are apt to be followed by chronic productive inflammation without exudate.

The effects of this type of inflammation vary with the structure of the tissue in which it is located.

In connective tissue the exudate infiltrates both the old and the new structures. The new growth adds to the thickness of the old, surrounds and compresses arteries, and forms irregularities on the surface or adhesions between apposed surfaces.

In mucous membranes the exudate infiltrates the stroma, is discharged from the surface, and a catarrhal inflammation of varying intensity is usually established. The new growth is regularly formed in the stroma, which is thickened, obstructs blood- and lymph-vessels, distorts and constricts glands, and causes atrophy of lymphoid cells. A mixed exudative and productive inflammation may be limited to the stroma of a mucous membrane with little or no catarrhal affection of the glandular layer.

In the viscera the stroma is the seat of a diffuse new growth replacing the parenchyma of the organ, while the exudate infiltrates the thickened stroma and the epithelial structures and is thrown off with the secretion of the viscus. The parenchyma

suffers a variable grade of degeneration and atrophy. The function of the organ is seriously and to some extent permanently impaired.

### (*c*) Chronic Productive Inflammation.

In chronic productive inflammation the new growth is regularly of the type of fibrous tissue. It may at first be comparatively cellular, containing fibroblasts and lymphocytes (round cells), or if of slower formation may have the characters of adult connective tissue, or may finally become densely fibrous. Under some conditions the blood-vessels may be numerous, and the tissue resembles granulation tissue. More often it is imperfectly vascularized, and tends to degenerate and soften or become calcified.

There is much controversy regarding the origin of the slow forms of chronic productive inflammation or chronic fibrosis. It appears to be due sometimes to a chronic irritant affecting the stroma of viscera, and at other times it appears to coincide with atrophy and degeneration of the parenchyma cells of the organ.

Chronic productive inflammation may be (1) chronic and continues from the first, but (2) it usually follows an initial subacute productive process and (3) frequently progresses with marked subacute exacerbations interrupted by periods of partial quiescence. During the exacerbations there may be exudation from the blood-vessels.

In connective tissue thickenings and adhesions are produced and there may be collections of serum, especially when the process affects serous membranes.

In mucous membranes the fibrous tissue of the stroma is greatly increased and there may be hyperplasia of lymphoid cells. Polypoid outgrowths often appear, sometimes reaching a considerable size. Some glands may become atrophic from pressure of the fibrous tissue, or cystic from constriction of their ducts, while the remaining glands may become hypertrophied. In

some situations the number and size of the glands may be so much increased as to resemble a true glandular neoplasm. The secretion of the glands may be increased as in the hypertrophic condition in chronic bronchitis, or diminished or absent as in atrophic rhinitis.

In the viscera there is a growth of connective tissue, sometimes infiltrated with round cells, beginning in the stroma and replacing considerable areas of the parenchyma. The blood-vessels are commonly sclerosed and deformed, or obliterated. The parenchyma cells are compressed and atrophic, or exhibit many stages and forms of chronic degeneration. Regenerative efforts on the part of the cells are sometimes a prominent feature. The functions of the viscus are seriously and permanently impaired.

## INFLAMMATION IN BONE.

Owing to the peculiar structure of bone and cartilage inflammatory processes here have some unusual features.

Bony tissue as such is incapable of exhibiting ordinary inflammatory changes and the inflammations which affect it are located primarily in the periosteum or the marrow.

It has already been noted that an exudative process of an intensity which would not prove necrotic in other situations may lead to extensive necrosis of bone by occlusion of the nutrient vessels, which, being inclosed in unyielding walls, are soon compressed by exuding serum or pus. Such inflammations are usually located in the periosteum. The dead portion of bone is slowly removed by a reactive inflammation proceeding along the line of demarcation from living bone, by a process which includes in order the following steps:

1. The absorption of calcium salts from a thin layer of bone surrounding the dead bone or sequestrum.

2. The development in this layer of a form of granulation tissue which is capable of exudative changes.

3. The development of a suppurative inflammation in this

locality which causes the further absorption and loosening of the sequestrum.

The absorption of bone is accomplished by the blood-vessels and through the instrumentality of certain large giant cells called osteoclasts. The complete extrusion of a large sequestrum is seldom accomplished without surgical interference.

When suppurative inflammation affects cancellous bone there is considerable absorption of many trabeculæ, which permits unabsorbed portions to break off in small masses or spicules. This process is called caries.

When chronic inflammation affects bone the common result is the gradual replacement of bone tissue with fibrous tissue, rarefying osteitis. At other times, or at certain points in rarefying bone, the process is chiefly formative, and new bone tissue of a dense variety is laid down. This is called sclerosing osteitis, or formative osteitis. In most of the specific chronic inflammations of bone (gout, rheumatism), both rarefying and sclerosing osteitis go hand in hand, and the shafts and joint surfaces become irregularly eroded and enlarged.

In tuberculosis of bone the changes are usually limited to the absorption and replacement of bone by granulation tissue, which commonly exhibits marked evidence of tuberculous inflammation. In chronic syphilis both rarefying and formative osteitis are often associated.

When chronic inflammation affects periosteum the connective tissues may be thickened but the osteoblasts on the inner surface of the membrane usually multiply and lay down irregular laminæ of new bone, causing deformities of the surface (inflammatory exostoses). These exostoses often grow to a large size and may be mistaken for tumors of bone.

When inflammation of any type affects the marrow of bone the process is called osteomyelitis. In the marrow the changes produced are similar to those occurring in other lymphoid tissues, while the effects upon surrounding bony structures are similar to those resulting from periostitis. Part II., p. 635.

# CHAPTER VII.

## NEOPLASMS.

A SPONTANEOUS, progressive, relatively functionless, non-inflammatory, development of new cells, more or less circumscribed, is called a neoplasm, and when it is specially marked by swelling, a tumor. Excluded from this definition are all collections of blood and inflammatory products and excessive development of a functionating part. If the tumor reproduces tissue which is normal in the organism it is said to be typical; if new or embryonic tissue, it is called atypical. Neoplasms are sometimes grouped according to their effect upon the patient as benign, when but little general damage is done, and malignant when the tumor tends to spread and cause profound constitutional disturbance. They are also classed according to the type of tissue in them or from which they have developed, and in the absence of more light on the subject this latter method, the histogenetic, is the most reasonable.

Several theories have been offered to account for the development of tumors, namely (1) that a portion of an embryonic tissue has been included in some other tissue and remains there until an exciting cause, as local injury, excites it to develop; (2) that an injury, without such a focus of included germinal tissue, causes superficial irritation; (3) that there is an infection by parasites peculiar to each kind of tumor. None of these holds

for all varieites of tumors and the parasitic origin is generally received only for the so-called infectious granulomata. Certain predisposing conditions are supposed to favor tumor growth, and heredity has been emphasized in the case of malignant tumors especially. Some tumors occur most frequently before adult age is attained, others afterward.

Tumors of simple structure, resembling the tissue in which they develop, are called homologous. Those whose structure is different from that of the surrounding tissue, and sometimes very complex, are called heterologous. It is the latter group which is explained by the theory of misplaced cells during the development of the embryo.

In external form tumors may be circumscribed, the new growth being contained in a fibrous capsule, or they may be infiltrating; the main histological distinction between these two is that the former grow centrally and the latter along the periphery, and clinically the latter are the more malignant. Tumors are said to be primary when first formed in a tissue, and secondary when occuring afterward elsewhere. They propagate directly along the continuity of the tissue; or by contiguity, as when a tumor of the uterus involves the intestine because that happens to lie against it; or by metastasis. Metastasis is the name given to the actual transportation of cells from the primary tumor to some other point, as when cancer of the cervix uteri is repeated in the breast or the lung. These cells pass through either the lymphatics or the blood-vessels. Carcinoma of the stomach may ulcerate, open venous radicles and cause thrombosis; from this malignant thrombosis emboli carried to the liver set up similar neoplasms where they lodge. Carcinoma mammæ is usually transported through the lymph circulation, or directly through the chest wall. Often, however, the neoplasm grows along lymphatic passages in a direction contrary to the lymph stream, the cells proliferating from the end of the neoplastic column in the line of least resistance, and also laterally, distending the channel.

The structure of tumors may be like that of any tissue in the body and may be made up of muscle, fibrous tissue or gland cells which elsewhere would be taken for normal; or they may contain chiefly cells which are normal only in the embryo. v. Anaplasia p. 63. Their blood-vessels are either like the normal or mere channels hollowed out through the substance of the new growth; nerves have been found in some forms other than in tumors of nervous tissue. When a tissue develops other than in its normal place it is called *heterotopous;* forming at a life period when it does not normally occur it is termed *heterochronous.* Tumor cells may deserve either or both of these adjectives.

In the microscopic diagnosis of tumors it is important to decide first if the tumor reproduces normal tissue; if not, then the relation between the stroma and the cells is of special significance. If a basement substance is made out between the cells it speaks for a diagnosis of sarcoma; if epithelial cells are found in groups (which are of course sections of long bundles or columns) without glandular arrangement or simulating gland acini, the probability is that the tumor is carcinomatous. The derivation of the new tissue is also of great importance, but in the atypical neoplasms the question is not always easy to decide. Microscopic examination of the edge of the tumor, where its cells are youngest, is often necessary to determine their origin. The more one type of tissue prevails the greater the probability that the tumor should bear the corresponding name, but mixed tumors may occur which in one portion resemble one type and in different portions another.

If localized and benign, the effects of a tumor may be merely an inconvenience, or more severe pressure and dragging. When malignant the general condition suffers from poisonous products, from invasion of important organs and the resulting disturbance of function, from pain, and from inflammatory changes in and about the new growths. Malignancy in the ordinary use of the term refers especially to the sarcomas and the car-

cinomas. Clinically the term includes multiplication of the tumor as well as local increase, pain and ulceration, and all the features of the cachexia. Histologically the diagnosis depends upon the destruction of natural boundaries by the rapidly proliferating cells, which are apt to have large vesicular nuclei and to show acidophile characters whether they come from fibroblasts or epithelia. The malignant tumor is apt to be very cellular, and its cells are large, atypical in arrangement, and have large nuclei, rich in chromatin. Mitotic figures are numerous. The invasion of adjacent structures is also usually demonstrable by the microscope. In proportion to their malignancy they return to the "embryonic" condition, in which their chief occupation was to multiply, and give up the functions of later acquisition; that is, the "habit of work" characteristic of the adult specialized cell is lost and only the accelerated "habit of growth" persists. Hence they do not pause in their multiplication and older cells are unable to resist them. The less this is noticeable the less malignant is the tumor.

Many tumors present various forms of degeneration in their cells, usually in the older portions, as colloid, mucoid, etc. From defective nutrition it frequently happens that new growths undergo necrosis, and this is peculiarly true of those which grow rapidly because their vascular supply does not keep pace with the increase of their cells. Tumors frequently grow more rapidly than the tisue in which they arise, and their nutritive demands are large. Occasionally a benign tumor becomes malignant by such changes, as when a subserous uterine myoma becomes twisted on its pedicle and undergoes necrotic softening from loss of nutrition; the fluid contents may escape and set up fatal peritonitis.

A tumor is named by adding to syllables indicating the tissue it resembles, the syllables -oma, which have been agreed upon as equivalent to tumor; in the case of sarcoma and carcinoma these words are retained entire with the tissue name prefixed.

# Classification of Tumors.

## A, 1.—Connective Tissue Tumors—Simple.

| Normal Type. | Typical Tumor. | Atypical Tumor. |
|---|---|---|
| I. Connective. | | |
| 1. Fibrillary. | Fibroma, hard and soft. | Fibro-sarcoma (desmoid) |
| 2. Wharton's jelly. | Myxoma. | Myxo-sarcoma. |
| 3. Fatty. | Lipoma. | Lipo-sarcoma. |
| 4. Cartilage. | Chondroma. | Chondro-sarcoma. |
| 5. Bone forming. | Ossifying fibroma. | Osteoid sarcoma (osteoblastoma). |
| 6. Bone. | Osteoma. | Osteo-sarcoma (chondro-osteo-sarcoma). |
| II. Vascular. | | |
| 7. Arteries. | Arterial angioma. | Plexiform angioma. |
| 8. Veins. | Caverous angioma. | Cavernous angiosarcoma. |
| 9. Embryonic vessels. | Nævus vasculosus. | |
| 10. Lymph vessels. | Lymphangioma cysticum and cavernosum. | |
| III. Muscle and Nerve. | | |
| 11. Smooth and striate muscle. | Leio- and rhabdo-myoma. | Myo-sarcoma; myogenic spindle-celled sarcoma. |
| 12. Embryonic muscle. | | |
| 13. Nerve, peripheral and central. | Neuroma verum; neuroganglioma. | Neuroma malignum (?). |
| IV. Connective tissue, rich in cells. | | |
| 14. Lymphatic. | Lymphoma, lymphadenoma. | Lymphosarcoma; myeloma. |
| 15. Neuroglia. | Glioma. | Glio-sarcoma. |
| 16. Endothelium. | Lymphangioma endotheliale. | Alveolar endothelioma. |
| | Perithelioma. | Fasciculate endothelioma. |
| 17. Pigment tissue. | Pigmented mole. | Melano-sarcoma, melanoma. |
| V. Placental. | | |
| 18. Decidua syncytium. | Simple deciduoma. | Malignant deciduoma. |
| 19. Chorion. | Placental polyp. | |
| | Simple mole, myxoma chorii. | Destructive mole, myxosarcoma chorii. |

## A, 2.—Connective Tissue Tumors—Compound.

| | | |
|---|---|---|
| 1. | Chondrofibroma. | |
| 2. | Myxolipoma. | |
| 3. | Fibromyoma. | Corresponding sarcomata. |
| 4. | Angiomelanoma. | |

## B.—Epithelial Tumors.

| Normal Type. | Typical Tumor. | Atypical Tumor. |
|---|---|---|
| I. Surface epithelium. | | |
| 1. Of skin, mucous membranes and papillæ of same. | Simple epithelioma, keratoma (horns), hard papilloma (larynx). | Flat celled carcinoma. Carcinoma of mucous membranes covered by squamous epithelium. |
| 2. Transitional and cylindric. | Papilloma cylindrocellulare (stomach, gut). | Cylindric celled carcinoma; papillary carcinoma of mucous surfaces. |
| 3. Ciliated. | Papillary cystoma (ovary). | Papillary ovarian carcinoma. |
| II. Glandular. | | |
| 4. Of tubular type (sweat, kidney). | Tubular adenoma (sweat glands, alimentary canal). | Adeno-carcinoma: glandular carcinoma in various glands with atypical alveoli. |
| 5. Of acinous type (breast, salivary). | Alveolar adenoma (mucous glands, breast, thyroid gland). | |
| 6. Of follicular type (thyroid gland). | Adeno-cystoma (ovary). | Adeno-cysto-carcinoma (ovary). |
| 7. Adrenal. | Hypernephroma. | Malignant hypernephroma. |

## C.—Mixed Tumors—Teratomata.

1. Typical tumors arising from inclusion of one or more embryonic layers.
   a. Dermoid cyst, part of ectoderm caught during infolding; tumor contains skin, hair, cutaneous glands.
   b. Cyst from cylindrical and ciliated epithelium; enterocystoma; branchiogenic cyst.
2. Mixed tumors arising from scattered parts of the germinal layers.
   a. Combinations of typical connective and gland tissue; fibro-adenoma, chondro-adenoma.
   b. Combined atypical gland and connective tissue; adenosarcoma; adeno-chondro-sarcoma; carcinoma sarcomatosum.
3. Mixed tumors representing rudimentary development of an embryonic layer (embryoma).
   a. Compound dermoid cyst of testis and ovary; parthenogenetic embryoma.
   b. Inclusion of rudimentary fetus in body cavity of a twin; fetus in fētu; parasitic embryoma.

# A. Simple Connective Tissue Tumors.

*Fibroma.*—Consists wholly of connective tissue with its vessels. Starts from fibro-blasts of nerve trunks, of vessel walls, of basement membranes, and connective tissue generally. Of two forms, hard and soft — the former resembling areolar tis-

sue, the latter made up of bundles of fibrous tissue woven tightly together. Soft fibromata are usually round, lobulated, may be enormous, develop in skin and subcutaneous tissue and leave the skin wrinkled after atrophy; may be pigmented and multiple; occur also from fascia, bone and retroperitoneal tissue.

Combinations, lipoma, myxoma, chondroma, sarcoma.

Hard fibroma; usually circumscribed, round, firm and tough, surface white and smooth on section, with concentric arrangement of fibers; grows slowly, may be multiple.

Occurs in fascia, periosteum, gland capsules, nerve sheaths. Combinations, myoma (frequent in uterus), cyst formation by softening, sarcoma.

*Microscopic.*—Soft; fibrous or homogeneous connective tissue with vessels, in large and fine mesh work, spaces filled with serous or mucous fluid. Hard; fibrous tissue in closely packed bundles, homogeneous or fibrillary, small collections of cells here and there, corpora amylacea frequent; veins may be irregularly dilated, like angioma.

*Keloid.*—A variety of fibrous new growth developing in the corium and presenting on the surface as small nodules and ridges. They have been called cicatricial when connected with a scar, and true keloid when spontaneous, but as a matter of fact they develop from injury always and are never spontaneous. Even a trivial injury will serve as a starting point in a patient who is disposed. They begin by proliferation of the fibroblasts along the small vessels, and reach deeply inward along their course as well as appearing on the surface. They differ from a cicatrix in always exceeding the limits of the wound, whereas a scar, even if hypertrophied, remains localized — is not a neoplasm, in other words.

*Myxoma.*— Usually round or lobulated, encapsuled or not, feels semifluid on palpation; section grayish, viscid, with fibrous bundles. *Microscopic,* basement substance mucous with round, stellar or spindle cells connected with each other by their poles; acetic acid precipitates mucin in fine reticular form. Occurs in

sheath of nerves and tendons, from fatty tissue, degenerated fibroma, and as polyps in nose and pharynx. Primary myxoma, which begins in embryonic indifferent tissue which later would form adipose or connective tissue, is exceedingly uncommon. The name secondary myxoma is applied to other forms when they suffer mucoid changes, as above.

Combinations, of especial clinical importance, with sarcoma.

*Glioma.*—Usually single, of slow growth from neuroglia, on reaching dura does not extend into it; from small focus to size of fist, grayish or yellowish, fairly firm. *Microscopically* contains round, spindle or multi-polar cells, may be bundles of fibrous tissue, vessels few or many, in last case frequent hemorrhages, may soften and become cystic.

*Lipoma.*—Roundish, lobulated, may be capsuled, soft but not fluctuating; on section areas of fat marked out by fibrous bundles clearly demonstrated; both the fat cells and the tumor lobules are larger than normal and not uniform in size; otherwise reproduces fat tissue. From overgrowth of normal fat or metaplasia of connective tissue; growth slow; in subcutaneous tissue, in joints, in fascia, may occur or persist in the emaciated.

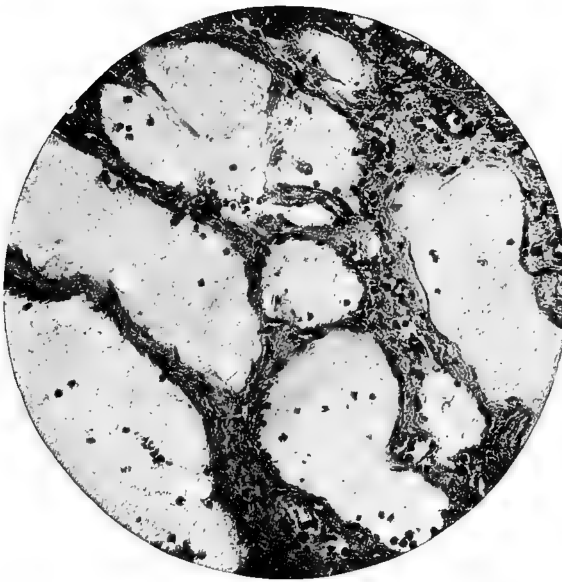
*Chondroma.*—May contain any kind of cartilage; called enchondroma if found in abnormal place as in testis, ecchondrosis if growing from cartilage and small. Usually hard, circumscribed, may reach large size; on section firm and homogeneous or hard and marked by fibrous bands; degenerates easily, forming cysts, or contains lime salts in quantity. May develop in endotheliomata and other tumors of the connective tissue group.

Combinations; lipoma, fibroma, myxoma, sarcoma.

*Osteoma.*—Bone tumors occur from inflammatory processes in the periosteum or as hypertrophies of normal bone, or in combination with other tumors. They are called osteophytes if small, flat, superficial deposits; exostoses if more localized, round and spur-like; parosteal osteomata if developed apart from bone.

The name osteoma is applied to bone tumors which are circumscribed, of steady growth, and made up of spongy or compact new bone tissue. Three forms are described, osteoma durum, spongiosum and medullosum, according as they are of hard bone, of spongy with a few marrow spaces, or with much marrow.

FIG. 25.



CAVERNOUS ANGIOMA OF THE LIVER. (PHOTO.)

Large irregular blood channels surrounded by compressed fibrous and hepatic tissue containing atrophic cells.

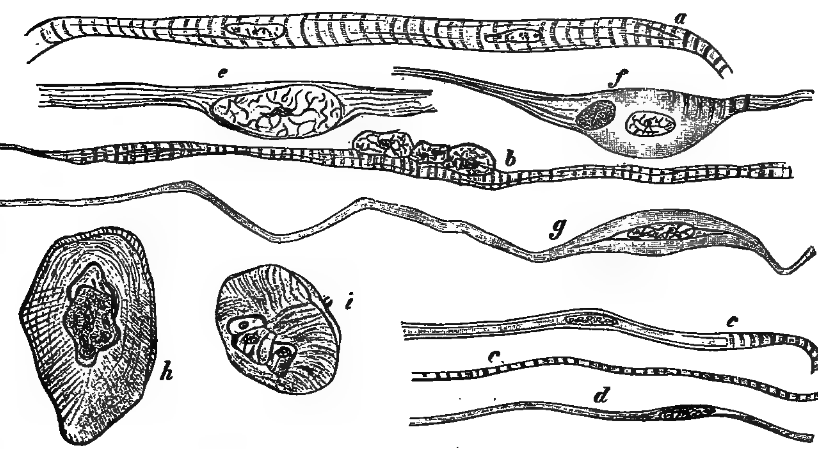
Occur from bones, at times after injury, cartilage, and fibrous tissues as pleura and diaphragm. Benign and of slow growth.

*Hemangioma.*—Consists of a small amount of connective tissue and great disproportion of vessels, newly formed and hence excluding varix and aneurysm; may increase in volume on

stimulus and then called erectile. Three varieties: telangiectatic, hemangioma simplex, or nevus, consisting of dilated capillaries; hemangioma arteriale plexiforme, of tortuous thick-walled arteries; and cavernous, like corpus cavernosum penis in structure.

*Myoma.*—Tumors of striated muscle cells are called rhabdomyomata and are among the most uncommon. Those of smooth

FIG. 26.




CELLS FROM RHABDOMYOMA. (*Ziegler.*)

*a, b, c,* striated muscle cells of varying thickness; *d,* slender smooth muscle cell, with nucleus; *e,* spindle cell, striæ longitudinal; *f,* spindle cell, striæ transverse; *g,* spindle cell with long processes, no striæ; *h, i,* round cells, striæ radiate or concentric.

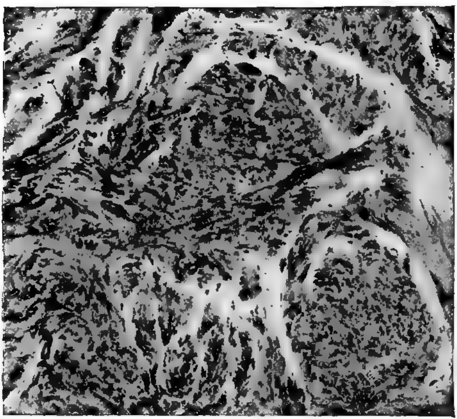
muscle tissue are called leiomyomata and occur in the uterus, intestinal canal, prostate and skin. They may be cystic or calcified, are usually of slow growth and benign.

Combination with fibroma common.

*Neuroma.*—This term includes (1) the true, or ganglionic, neuroma made up of nerve cells and their fibers, with glia cells;

(2) the glioma, already treated; (3) and the false neuroma, which develops along nerve trunks from their fibroblasts. The first is found in the brain and teratomata. The second is common in the brain and the retina. The third is often multiple, richly cellular, or fibrous when older.

Fig. 27.



Leiomyoma of the Uterus. (Photo.)

Islands of muscle fibers mapped out by light bands of fibrous tissue.

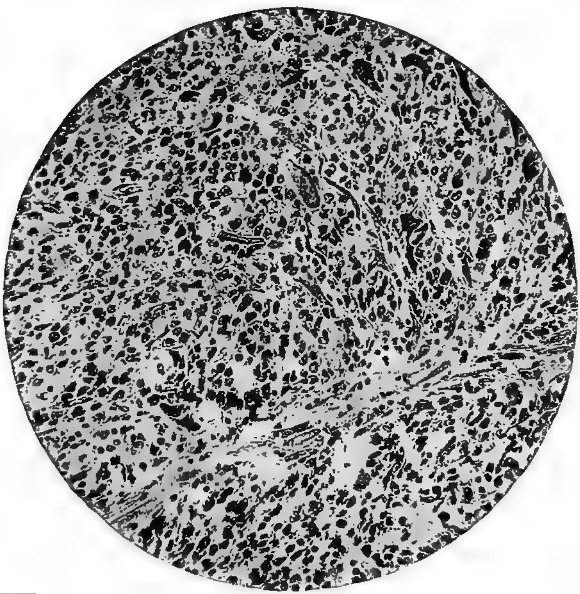
## B. Tumors from Connective Tissue with Excessive Cell Formation.

*Sarcoma.*—Tumors developed from connective tissue, with the stroma disproportionately sparse and the cell formation excessive and tending to progress, the cells having an embryonic or imperfectly formed character, are called sarcomata.

Sarcoma may develop from any of the tissues grouped under the name of connective, and often displays analogies with the special kind from which it is developed; thus sarcoma in the choroid tunic of the eye often forms pigment, and in the

periosteum, bone. The relation to connective tissue may be recognized also in the fact that the tumor cells are closely connected with each other and even when most richly present tend to form fine intercellular substance, which can be demonstrated by proper staining methods. In one sense, then, we may speak

FIG. 28.

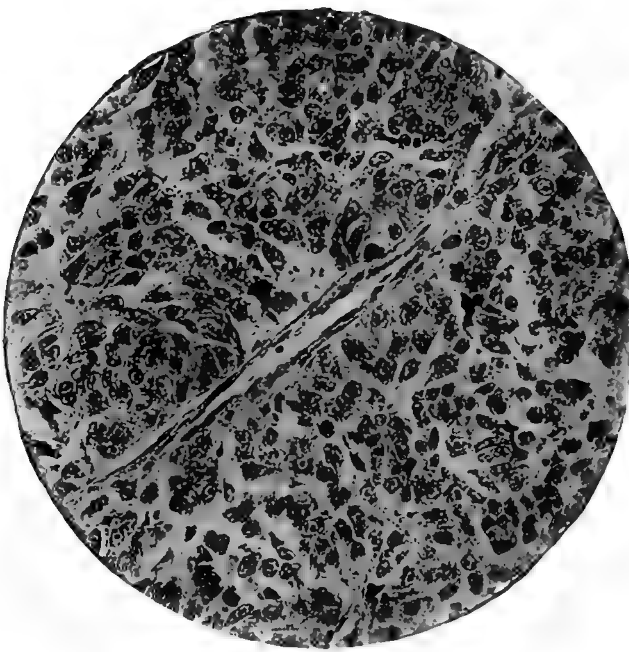


SMALL ROUND-CELLED SARCOMA. (PHOTO.)

of the stroma and the parenchyma of such tumors. The commonest forms of cell formation found in them are the round, resembling lymph cells or exceeding them in size, the spindle form of varying sizes, star-shaped, and giant cells. The intercellular substance is either fibrillary, granular, homogeneous or reticular and varies within wide limits in proportion to the cells. It may be so scanty that special stains (as Van Gieson's)

and the higher powers of the microscope are required to recognize it. The vessels may be so many and large that the tumor is cavernous, and most often a peculiar relation between vessel wall and cells may be recognized; the cells are closely applied

FIG. 29.



LARGE ROUND-CELLED SARCOMA.

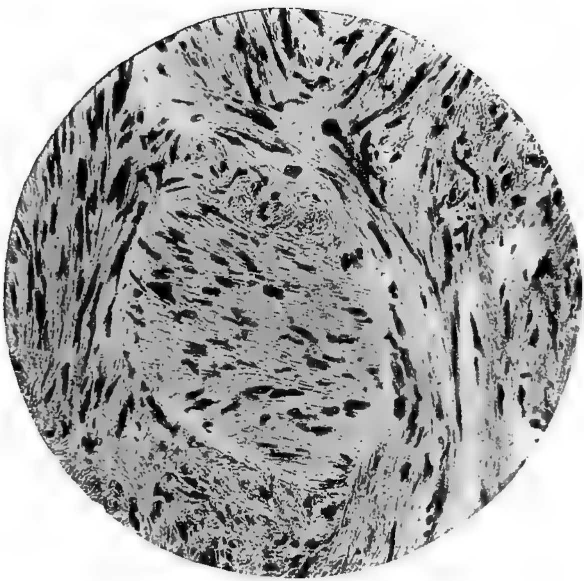
to the vessel with only faint indications of a wall, or the blood channels are simply tunneled through the tissue. Hemorrhage from the vessels in sarcomata is common.

Varieties. The kind of cells predominating determines the kind of sarcoma:

1. *Round-celled sarcoma* may be of either the small- or

the large-celled variety; the small-celled resemble granulation tissue and have but little stroma. In the gross they are soft, the cut section gives a milky juice on scraping; they grow rapidly, are not encapsuled, form many and early metastases and are among the most malignant; from connective tissue

FIG. 30.



FIBRO-SARCOMA. (PHOTO.)

of muscle, fascia, bone, testis, brain, etc. Large round-celled sarcoma differs chiefly in the size of the cells and the occasional alveolar arrangement. These cells are derived from fibroblasts. They are called large round cells but their actual outline is

quite as often polygonal. Some lympho- and melano-sarcomas belong in this class.

2. *Spindled-celled sarcoma,* also divided into large- and small-celled, one of the commonest sarcomas; resemble muscle cells if large; may lie closely packed or appear as a fibrillar stroma between bundles of spindle cells; develop from fibroblasts or their derivatives in any tissue.
3. *Giant-celled Sarcoma.*—The main tumor may be of any kind but with the other cells there occur giant cells, large spheres of protoplasm with many centrally grouped nuclei, often oval shaped. Such giant cells are commonest in sarcoma developing from periosteum and bone. In the giant cells of the infectious granulomata and those formed about foreign bodies the nuclei may be arranged as a crescent at one pole of the cell or as a complete peripheral ring. Their longer axes may coincide with the radii of the cell. This type is known as the Langerhans giant cell and is distinguished from the myeloid, whose nuclei are central.

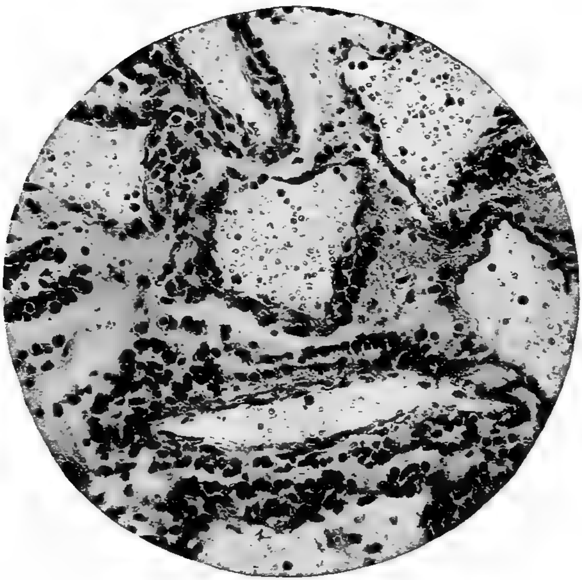
Grouped according to the variety of the connective tissue which forms their foundation and origin, sarcomas are described as: fibro-sarcoma, myxo-sarcoma, glio-sarcoma, chondro-sarcoma, osteo-sarcoma, melano-sarcoma, myeloid sarcoma, lympho-sarcoma, myo-sarcoma, neuro-sarcoma, and angio-sarcoma.

These tumors grow rapidly in proportion to their cell contents and the size of the distinguishing cells; of them all, those with small round cells grow most quickly. Their nutrition, because of the many and relatively large vessels and their relations, is very free. Fibro-sarcoma may be encapsuled, other varieties seldom, but even with a capsule the tumor grows through and beyond it, increasing peripherally, pushing between other elements and replacing other tissues. The very cells of the capsule

themselves become sarcomatous. They may remain stationary for a time and then suddenly increase in size or grow rapidly to large size from the start.

They are very prone to degenerate, hence every form of necrotic and softened area and consequent cystic formation may

FIG. 31.



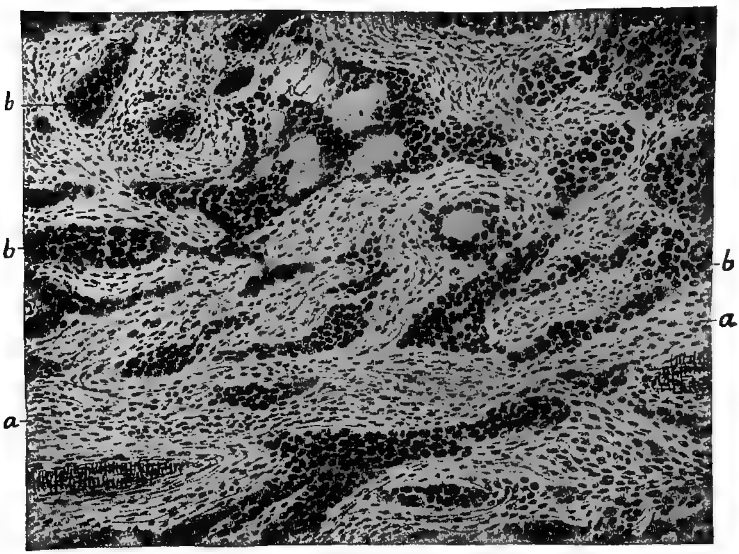
ANGIO-SARCOMA. (PHOTO.)

A tumor of this type has always been called angio-sarcoma; a better name perhaps would be angio-endothelioma.

occur. On the surface of the body they break down and form ulcers. When a hyaline degeneration involves the blood channels, converting them into swollen cords and decreasing their lumen, the tumor is called a cylindroma. When modified fat pigment gives the tumor a green color it is termed chloroma.

Their malignancy is seen in their rapid growth and invasion of parts directly, frequent metastasis (most often through the blood-vessels), and prompt recurrence after operative removal. Constitutional depression is perhaps not so marked as in carcinoma. With multiple metastases all through the body the

FIG. 32.




ENDOTHELIOMA OF PLEURA. (*Ziegler.*)

*a*, fibrous stroma; *b*, endothelial cells proliferating along lymph spaces in strands and columns.

dissemination is spoken of as a sarcomatosis, as the similar condition in cancer is called carcinomatosis.

The etiology is more clearly dependent upon late development of fetal remnants than in the case of some other tumors; to which opinion the occurrence of congenital sarcoma, and the development of simple and complex sarcomas of the testis,

parotid gland and thyroid, of heterotopous nature lend probability.

*Endothelioma.*—Proliferation of endothelial cells is comparatively common in some tumors. At times the cells are collected in heaps and bundles, sharply marked off from the stroma. Such tumors have been grouped with carcinoma and then with sarcoma. But in carcinoma the relation between the epithelium of the tumor and the epithelium of the tissue of origin is demonstrable, and the relation of the cells of a column in a lymph space to the wall of the space is so loose that they retract from it in hardening; while in endothelioma the cells are organically connected with the intercellular stroma derived from them, and in the case of many endotheliomas the derivation of the cells from the endothelial cells of the part has been observed. The endothelial tumors appear to belong to the connective-tissue group because transitions and combinations frequently occur between them and other tumors of this class, both typical and atypical. Possibly the same stimuli which cause the endothelia to proliferate produce like effect upon the fibroblasts of the part, or conversely.

Quite frequently endothelioma begins in the finer lymph spaces of connective tissue or in the walls of lymph channels. These tumors occur in several forms, namely, interfascicular, plexiform, perivascular, diffuse and alveolar. These forms are chiefly dependent upon the nature of the tissue in which the endothelial proliferation starts, especially with reference to the lymph spaces. If made up of firm fibrous bands, running chiefly parallel, the lymph channels and radicles have the same general disposition, and the new cells make their way along them and form the fascicular type. Here lines of single cuboid cells lie in long narrow spaces, often more than a hundred, one behind another, the terminal cells at each end being longer. Where the lymph spaces form a close network, with fine or coarse meshes, the tumor is plexiform. When the cell multiplication is rapid and the opposing pressure but slight, the walls of

the spaces are pressed apart and the alveolar type is assumed. The cells in the alveoli may be flat, cuboid, or columnar. The other names are self-explanatory. Endotheliomas have been found in the cerebral membranes, marrow, testis, ovary, lymph nodes, etc.

A special form of endothelioma occurs as a superficial thickening of serous membranes, or as little spheroids scattered over them, and may strongly resemble such membranes when thickened by chronic inflammation. Metastasis may occur in the lung, liver, muscles, and elsewhere.

A form of deeply pigmented tumor, called *melanoma,* occurs in the choroid and the skin, where pigment normally occurs, and very frequently in relation with pigmented moles. It may develop from the palisade cells of the rete Malpighi, which proliferate toward deeper structures, and may or may not be snared off from their point of origin. In this case the tumor is an epithelioma. They may, however, take origin from endothelia of minute blood and lymph-vessels in the rete. This would make them endotheliomata. They are often very malignant and rapidly spread by metastasis.

## Tumors Resembling Sarcomata. Syncytioma, Mixed Forms.

*Syncytioma or Deciduoma.*—Simple and malignant tumors may develop from the decidua, or from hydatid moles, after interrupted and normal pregnancies, immediately or after long intervals of time. Many are of rapid growth, degenerate easily, form metastases in vagina and lung especially, and are extremely malignant. Three forms of cells are found; large epithelioid, with nuclei rich in chromatin, arranged in network with wide blood spaces between; small, polyhedral, rich in glycogen, in masses between the other kind; and many forms transitional between these. By some authors this tumor is considered an epithelioma.

*Mixed Forms.*—Mixed sarcomatous tumors occur in the parotid and thyroid glands, in the ovary and the testis, and contain mucous, vascular, cartilaginous and other elements. They may be referred to inclusion at the point of origin of embryonic cells already differentiated, which are held in an undeveloped condition till some stimulus causes them to form tumors. They are usually teratomata and not simple tumors.

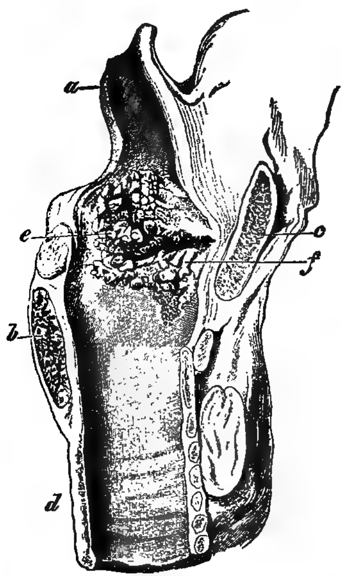
## C. Tumors of the Type of Superficial Epithelium.

Simple hypertrophy of the epidermis may occur as the result of repeated slight irritation. Apart from such growth there are several forms covered by the name papilloma, verruca, condyloma, etc.

*Papilloma.*—This is made up of connective tissue and its vessels and is covered by a single or multiple layer of epithelial cells, and the physiological type is found in the papillæ of the skin and the villi of the intestine. The variety of the epithelial covering differs with the site of origin and attachment of the tumor. The vessels may be divided into loops corresponding each to a subdivision of the tumor or they may form networks of great complexity; the whole may be compared to a tree of connective tissue with frequent branches, which vary much in size and are clothed with a layer or two of epithelium. Sometimes the normal papillæ seem merely to enlarge, at others they branch as stated. In the gross there may be countless small tumors, or one or two mounted on pedicles, or a small area covered with the fine subdivisions on a common base. The color and density depend upon the thickness of the epithelial layer, the amount and kind of connective tissue and the richness in vessels. Papillomata are divided into the hard, embracing those of the skin covered with cornified epidermic scales and of the mucous surfaces covered with pavement cells, and the soft which are often covered with modified cylindrical (ovoid) epithelium and are found in hollow viscera. Common

examples of the hard papilloma are the warts found on the fingers about puberty, cornu cutaneum, and pointed condylomata (the latter seem at times to be contagious, both in man and the lower animals). Soft papillomata have a stroma richer in cells and vessels than the hard and seldom present horny

FIG. 33.




PAPILLOMA OF LARYNX. (*Ziegler.*)

*a*, epiglottis; *b*, cricoid cartilage; *c*, thyroid cartilage; *d*, trachea; *e*, false vocal cord; *f*, true vocal cord, both bearing papillary outgrowths. Between them is the opening of the sinus of Morgagni.

epithelia on the surface, the usual covering is that of the part where they grow, though cylindric cells may be found in papilloma developed among squamous. They occur frequently in the bladder, rectum, uterus and vagina, less often in the breast (ducts), gall-bladder and ependyma of brain ventricles; com-

binations with carcinoma are found. They are dangerous because of their tendency to bleed.

## D. Tumors of the type of Gland Epithelium.

### Adenomata.

Transitions from enlarged glands to adenomata are frequent and hard to define, and on the other side the adenomata fade into the true carcinomas. Adenoma may be defined as an independent new formation reproducing typical glandular tissue, made up of connective tissue arranged about spaces which are lined by epithelium. While these epithelia are not strictly functionless — for no living cell can be so regarded — yet as concerns the organism they probably do not aid in constructive metabolism. Adenoma may usually be recognized by the unaided eye, by its different appearance from normal gland and by its circumscribed form, often being encapsulated by fibrous tissue; the picture of the hypertrophy of functionating glands, as breast and kidney, is a very different one, as also of glands swollen by confined products.

Adenomas developing in gland or from scattered fragments of embryonic tissues will usually be found encapsuled, seldom diffuse, and on surfaces are usually broad or polypoid. Two types are found according to the prevalence of tubular or acinous arrangement of the alveoli; the former on mucous surfaces and in the ovary, the latter in the breast. The adjective heterotopous is applied to adenoma which develops apart from normal glands or in glands but of an abnormal type, as a papillary adenoma in the kidney which does not correspond with renal structure. Adenoma may arise from embryonic fragments which develop wrongly later, or from misdirected repair and hypertrophy after inflammations; the latter form leads directly to carcinoma in some cases. Certain of the primary carcinomas of the liver may be thus explained.

The main distinction between adenoma and carcinoma is

found in the typical character of the former as contrasted with the atypical alveoli of the latter, although as compared with normal gland the adenoma is not physiological. Thus in glands of acinous structure we may find the adenoma developing tubular glands, and instead of a single layer of epithelium there may be two or more, perhaps cuboid and with papillary outgrowths.

FIG. 34.

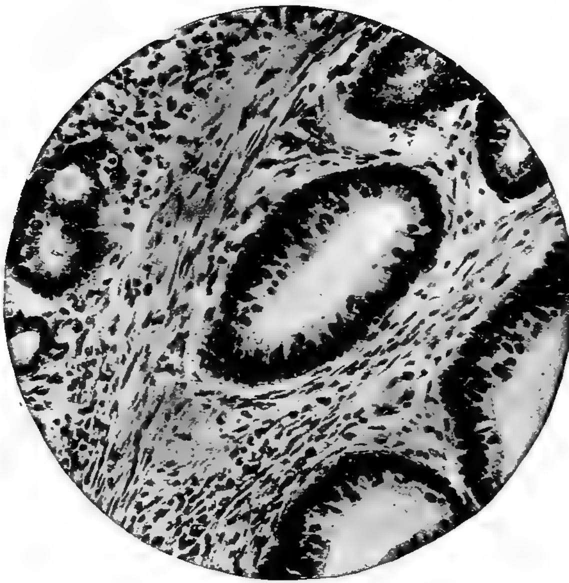
ADENOMA OF THYROID. (PHOTO.)

But in contrast with carcinoma, the new-formed cells lie in actual gland spaces and are distinctly separated from the basement substance, often by a membrana propria.

The usual degenerations, fatty, mucoid, and colloid, may occur in adenoma, and hence the tumor can be cystic; by the pressure exerted thus from within, the walls of adjoining spaces disappear and thus the tumor becomes lobulated (adenocystoma).

Though usually benign, except for mechanical effects, adenomata may break into blood and lymph channels and cause metastasis, and especially in the alimentary canal they develop at the expense of the submucous tissues, grow rapidly and are

FIG. 35.



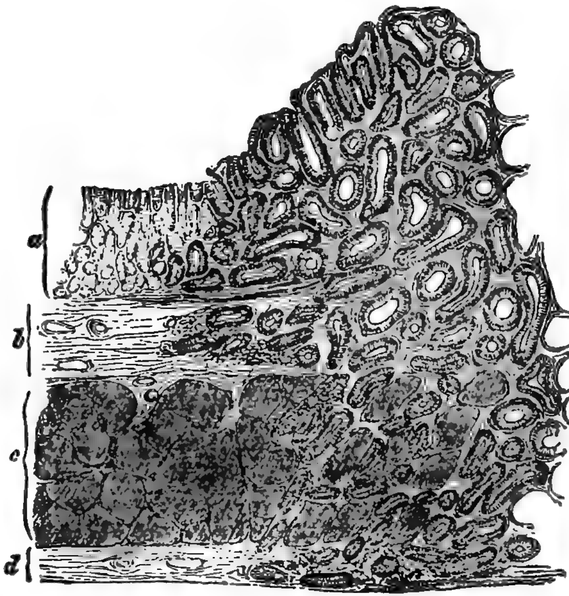
ADENOMA DESTRUENS. (PHOTO.)

A cellular stroma enclosing gland acini which are lined by several layers of epithelial cells. Both acini and epithelia are atypical, but the cells do not transgress the limits of the acini and invade the stroma.

clearly malignant (adenoma destruens of stomach, gut and uterus). Such a tumor may be considered as an adenoma which has become carcinomatous. Combination with sarcoma is also found; here it is the stroma which is especially affected by the cellular hyperplasia.

*Hypernephroma.*—Occasionally adenomas develop in the abdominal organs, especially kidney, liver, and internal genitals (broad ligament), which reproduce the structure of the adrenals; they are evidently due to the late development of

FIG. 36.




MARGIN OF AN ADENO-CARCINOMA. (*Ziegler.*)

*a*, mucosa; *b*, submucosa; *c*, muscularis; *d*, serosa; *e*, neoplasm starting in the mucosa and invading all the other coats. Diagrammatic.

scattered portions of adrenal tissue, which have been found in the abdominal sympathetic ganglia also. (*v.* Pt. II., p. 534.)

## E. Atypical Epithelial Tumors.

*Carcinomata* are neoplasms made up of connective and epithelial tissues arranged atypically, the latter often multiplying

by atypical mitosis and always having a tendency to transgress normal tissue-limits.

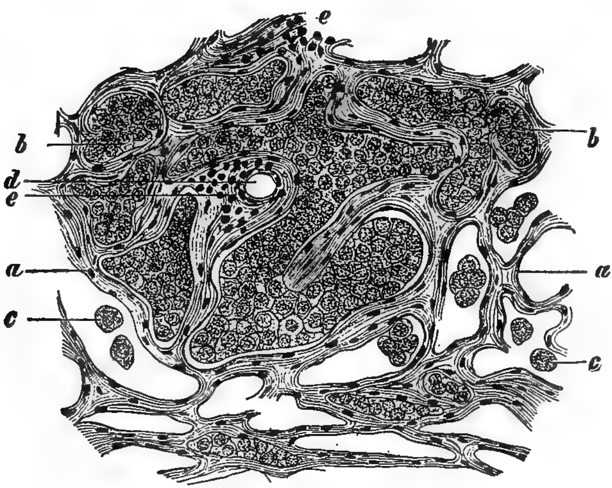
The cells in this group of tumors are the characteristic element rather than the stroma, and still it must be remembered that there is no uniform cancer cell — no cell which apart from its environment would always be demonstrable as a cancer cell. Yet in their usual sites of growth they may be at once recognized. From their resemblance to normal epithelia they are called epithelioid. They may be many times larger than any normal epithelial cell; their nuclei may be large and vesicular and stain so intensely that it is evident that their chromatin differs from that of the normal cell, a condition known as hyperchromatosis. They may multiply by atypical mitosis, showing tripolar and multipolar forms and irregular or superfluous monasters and diasters. These two characters are related to their extremely rapid proliferation, which in turn is one of the elements of their malignancy. When rapidly formed in a part where they are not subjected to much pressure the cells may be small and round, the protoplasm in relatively small amount. By mutual pressure they take on polygonal outlines, and when compressed by firm fibrous tissue they may have one axis much longer than the others. Under some pressure conditions, or when the nuclei multiply at a faster rate than the protoplasm, giant cells occur.

In apparently normal glands where the cells are beginning to take on the atypical character, often the first observed variation from the normal is their rapid proliferation, the acinus being then lined, it may be only at one point, by a double or triple layer of epithelia.

Tumors of this group exhibit many variations in form, consistence, gross appearance and anatomical relations; they may be very hard if containing much fibrous stroma (scirrhous), or soft and resembling brain tissue when very rich in cells (medullary). According to such circumstances and the kind and size of the cells, the microscopic picture also is varied. The frame-

work of the tumor is made up of new connective tissue, and mingled with it, unlike any normal adult tissue, are groups and strands of epithelia, arranged in solid bundles or lining alveoli in one or several layers. The form of the cells depends upon the tissue of origin, those in superficial cancer of the skin resembling epidermis cells, those from the primary carcinomas of the liver copying the liver cells or the epithelia of the bile

FIG. 37.



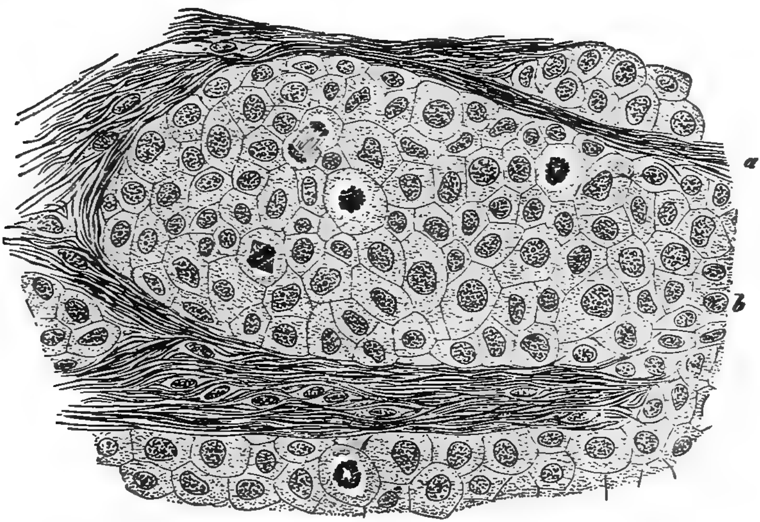

CARCINOMA SIMPLEX. (*Ziegler.*)

*a*, fibrous stroma; *b*, cylinders of cancer cells cut at various angles; *c*, single epithelioid cells; *d*, blood-vessel surrounded by fibrous tissue; *e*, round cells.

capillaries. After the tumor has developed there is a polymorphism of the cells which carries them much farther from the normal; if rich in protoplasm, they are soft and easily altered by pressure, so that round, spindle, polygonal and irregular cells at times coëxist in the same part. Further, as degenerative changes are common, these also modify the appearance of the cells.

The stroma may be partly derived from the region in which the tumor develops and partly from new connective tissue; occasionally muscle, fat, or gland tissue remains in the tumor for a time. All varieties of stroma are found, from young granulation tissue, rich in cells, to spindle-celled and fibrous; it grows with less energy than the epithelial cells and presents few mitotic figures. Plasma cells also are found and when

FIG. 38.




CARCINOMA MAMMAE. (*Ziegler.*)

*a*, fibrous trabeculæ; *b*, large atypical epithelia of polygonal outline, showing mitotic figures.

the tumor suffers the changes due to irritation and inflammation, lymphocytes and polynuclear leucocytes occur. In carcinoma connected with bone, plates of ossification may be found and giant cells as in sarcomata.

The relation of the tumor to the neighborhood in which it grows varies with the rapidity of its growth, and that varies

with the kind of cells present and the amount of stroma; but all such tumors infiltrate neighboring tissues by extremely fine peripheral processes, so that the apparent gross limit of the tumor is often not the real edge of the neoplasm and in operative removal there is danger of leaving behind small foci from

FIG. 39.

COLLOID CARCINOMA. (PHOTO.)

The lighter areas are masses of cells which have undergone degeneration, leaving scattered groups which still stain.

which the tumor will develop anew. Thus in cancer of the breast the skin may be interruptedly involved, and present minute nests of embryonic epithelia at a distance from the main tumor. These foci, at times hardly visible in the gross, are the starting points for recurrent tumors. They may have

spread laterally through the cutaneous lymph channels; but the skin may become involved from below also, lines of proliferating cancer cells from a more deeply seated tumor following lymphatics against the stream. Slowly growing carcinoma is apt to be fibrous, hard to the touch, and as the fibrous tissue contracts it dimples the surface, as in some carcinomas of the breast. Beside the local growth, metastasis is common by way of the lymph channels, and at times through the blood-vessels also. The secondary tumors so formed usually reproduce the character of the primary.

Degenerative changes are more common than in normal epithelium, but while the center or the surface may degenerate the tumor persists in its peripheral development and only as an exception is the regressive change a healing process. Either the stroma or the cells may degenerate, and there is an apparent correspondence between such changes and the part where the tumor occurs; breast cancer often becomes fatty, in the mucous tissues mucoid change is common, and in the thyroid gland, colloid. Such a relation seems to point to a partial conservation of the function of the epithelia, as when cancers of the liver contain bile, and those of the breast colostrum. Much that is called colostrum, however, is but masses of fatty degenerated epithelia derived from the duct wall. Traced back to the acini there is no relation between these and the "colostrum."

Fatty degeneration of a cancer resembles similar alterations elsewhere. The fat may occur in large meshwork and give the tumor a yellowish look and softer consistence; after resorption of the fat the tumor shrinks.

Mucoid degeneration may be like that observed in other tissues, or may be a solution of the cells in a viscid pseudo-mucin; hyaline and myxomatous degeneration may be observed in the same tumor; when well marked there are in the gross small grayish semitranslucent points or cyst-like cavities filled with sticky fluid. The highest grade of this degeneration, as often encountered in the carcinomas of the stomach and gut, has

been considered a special variety and received the name gelatinous or colloid carcinoma. Often such a tumor has an alveolar structure which may be recognized by the unaided eye. Because of the degeneration of the epithelium and reduced energy of the neoplastic process, these tumors make but few

Fig. 40.

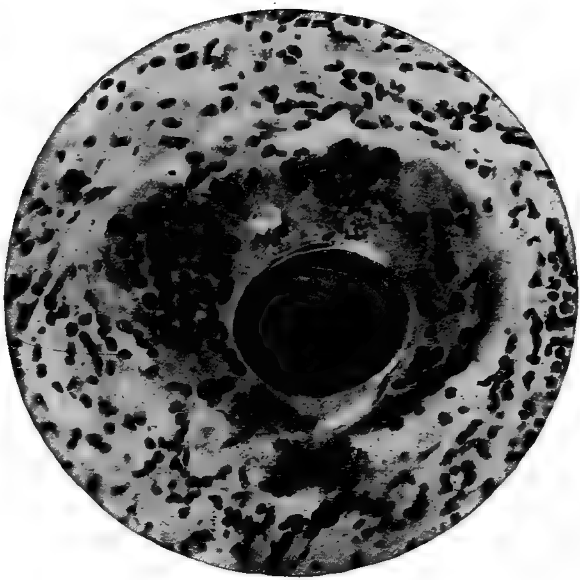
Rodent Ulcer. (Photo.)

metastases and grow slowly. Owing to disturbance of the tumor's nutrition liquefaction and other necroses may occur.

*Rodent Ulcer.*—On skin and mucous surfaces carcinomata almost invariably ulcerate and discharge thin, foul-smelling fluid. The edge of such an ulcer is usually thickened by the advancing epithelial growth, and looks like a sharply cut wall on the ulcer side and slopes gently away on the sound side. A

rodent ulcer and an epithelioma which is ulcerating may resemble each other, but in the former there is no cornification of the epithelia (hyperkeratosis) and its growth is very slow. Moreover, it starts in the basal layer of the epithelium and its

FIG. 41.



EPITHELIOMA. (PHOTO.)
Large whorl of laminated corneous epithelia surrounded by non-corneous cells. Several myeloid giant cells shown.

cells remain embryonic, while in contrast to this the cells of epithelioma return to an embryonic state, but afterward may resume their tendency to make cornified scales, hence the pearls or whorls so common in the latter but never seen in rodent ulcer.

Beside the degenerations mentioned, local collections of horny epithelia occur in cancer of the skin and mucous surfaces

(tongue, cervix uteri, etc.), as onion-like, laminated spheres lying deep in the epithelial processes as in a lumen, with other epithelial cells packed closely round them. Calcification and pigment are not common in carcinoma. Hemorrhages in the tumor occur when cell growth is very free or after vessels are eroded by ulceration. Cysts may form from such hemorrhages or from softening and degeneration. Combinations occur with other tumors and with gumma and tubercle tissue, but not often.

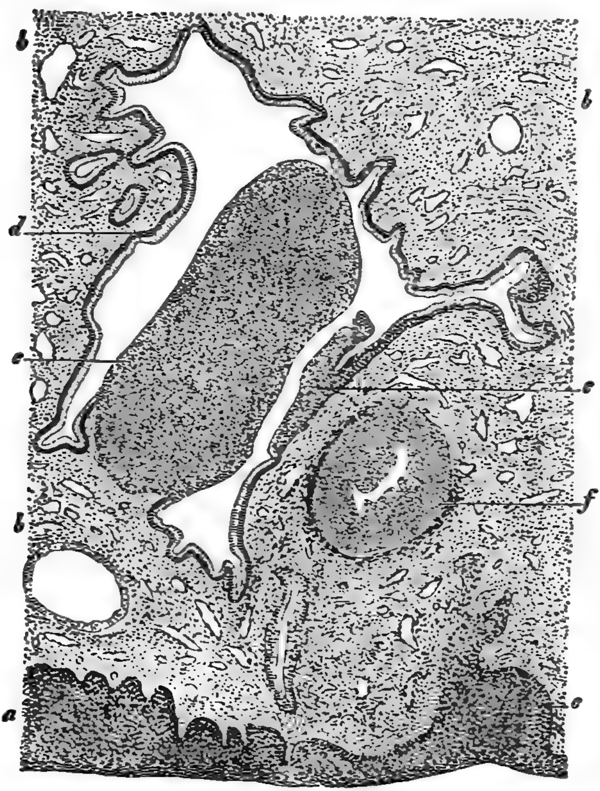
Carcinomata have been classified as scirrhous, encephaloid, colloid, etc., chiefly from their gross appearance, but a division according to the nature of the epithelial element and the type of gland represented is to be preferred. Thus we have flat-celled and cylindrical-celled carcinomas, adenocarcinoma and carcinoma glandulare solidum.

*Flat-, Squamous- or Pavement-celled Carcinoma.*—For this variety the name *epithelioma* is usually employed. It is found where flat epithelia normally exist, as the skin and mucous surfaces. It develops especially at lines of junction between skin and mucous membrane, as on the lip, the ala of the nose, the eyelid, glans penis, labia and portio vaginalis. It begins as an induration, usually not deep, circumscribed but vaguely; ulceration occurs early and may be rapid. The microscope shows large or small epithelia like those of the part which reach down into the tissue in straight or branching bundles, many of these exhibiting the whorls or pearls or cancroid bodies of tightly packed horny cells. The term hyperkeratosis is used for the marked cornification of the epithelia, not only on the surface but deep in the intruding columns as well. This return to the type of corneous scales, as soon as the column stops growing, explains the formation of the characteristic pearls. These are laminated and tightly packed because of the pressure of surrounding tissues. Their presence is not essential to a diagnosis of epithelioma, for in a rapidly growing tumor proliferation may be so steady and continuous that there is no time, so to speak, to produce whorls. When the tumor starts in the

prickle cells of the skin, and the cells preserve these processes, the special name *acanthoma* is sometimes applied to it.

*Cylindrical celled epithelioma* occurs especially in mucous

FIG. 42.




BEGINNING CARCINOMA OF PORTIO VAGINALIS. (*Ziegler.*)

*a*, superficial epithelium; *b*, fibrous stroma with vessels and lymph spaces; *c*, cone of epithelium invading the deeper tissues; *d*, mucous gland irregularly dilated; *e*, its epithelia proliferating in many layers and forming a large plug which protrudes into its lumen; *f*, gland cut across, showing less dilatation but the lumen nearly filled with atypical epithelia.

membranes which have one or several layers of cylindric epithelium; the stomach, rectum, bile capillaries, cervix and corpus uteri are often involved; if cilia are normally present in the epithelia of the part the tumor cells may reproduce them but usually not. If it starts deeply in the mucous crypts of an organ it remains for a time as a broad infiltration, but soon it reaches the surface and presents an ulcerating appearance. Heterotopous tumors of this kind may occur in the kidney, thryoid, bones and peritoneum. Microscopically the tumor is arranged in acini clothed with a layer of cylindrical cells, often two or more layers at some points, supported by varying amounts of stroma, which may be degenerated; later the cells may fill the acini to distention.

*Carcinomata reproducing gland structure* are called adeno-carcinomata and are common in the stomach, especially at the pylorus, the testis, ovary, uterus, breast, prostate and pancreas. They are described as occurring in the three forms of simple, medullary and scirrhous, according to the amount and proportion of epithelia and stroma; practically the three forms are modifications of the same tumor. If simple, the proportion of stroma to cells is about as in most glands; if medullary the cells are in excess and the tumor is soft; if scirrhous the fibrous stroma is so developed that the tumor is very hard, and even under the microscope careful search is required to detect epithelial cells, and thus its true nature, except in the younger portions. This form may be either nodular or diffuse; on scraping a cut section with a knife a milky fluid is collected, made up of degenerated epithelia, and fat, in an albuminous fluid. The tendency to mucin formation is strong.

*Paget's Disease.*—Beginning as a quasi eczema of the nipple, the later stages of the disease are ulceration and a carcinomatous process, the epidermic cells showing inflammatory changes, vacuolation and edematous infiltration of nucleus and protoplasm. From its resemblance to other superficial malignant tumors it has been considered as a special form of flat-celled

epithelioma. Because of the apparent presence of coccidia in the cells (vacuoles) it has been interpreted as a cancer in which the parasitic etiology is clear. The parasite is said to occur as small protoplasmic bodies which are at first free in the tissues, but then they enter epithelial nuclei, or protoplasm. They develop further at the expense of the cell to sporozoa, and the

FIG. 43.

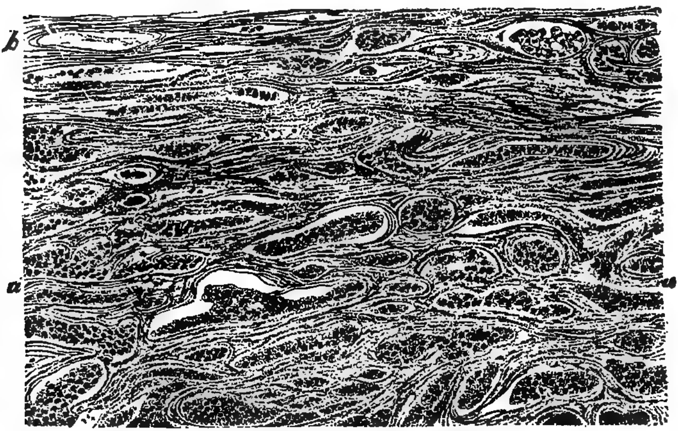
PAGET'S DISEASE. (PHOTO.)

nucleus divides and subdivides to form sporozoites, which are thin and slightly curved filaments. This parasitic explanation is not generally accepted.

Clinically the course of carcinoma is usually slow, requiring months or years before general symptoms occur; but the rapid increase (from increased nutrition) in uterine cancer after the

establishment of pregnancy is an example of the effect of local causes in hastening the disease. When the growth and metastasis are rapid a profound cachexia develops which may be due either to the symptoms, as pain, the exhausting discharges from ulcerating points, the disturbance of glands by the formation of secondary tumors, or the absorption of some peculiar toxic substances from the misdirected function of the newly

FIG. 44.




TUBULAR SCIRRHUS. (*Ziegler.*)

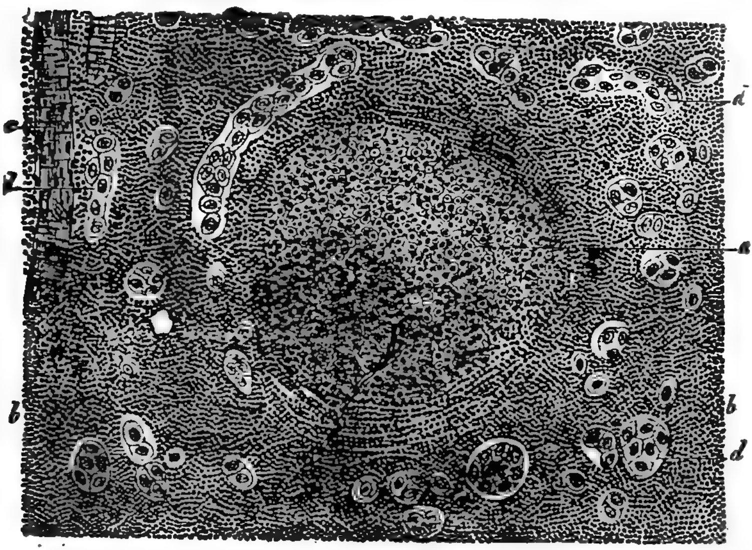
*a*, variously shaped columns of epithelia cut at different angles; *b*, cells disappearing, stroma beginning to predominate.

formed epithelia. The quantity of nutritive material of which the organism is robbed by the tumor is probably not a factor of importance in the cachexia.

The cause of carcinomatous formation is still a matter of uncertainty. Many influences of an irritative nature are noted, as in epithelioma of the under lip perhaps connected with the habit of smoking, but the upper lip which seems as much exposed commonly escapes; and age has an influence, for the majority

of cancers occur after the fortieth year, when the tissue resistance throughout the body is beginning to diminish with the approach to senility; the sex plays a part, for more women are the victims of cancer than men, although the occurrence of cancer on the skin and in the alimentary canal is more common among men: but no one of these nor all of them will explain

FIG. 45.




METASTATIC CARCINOMA IN LYMPH NODE. (*Ziegler.*)

*a*, mass of young cancer cells; *b*, lymphoid tissue of the node; *c*, small artery; *d*, fully developed atypical epithelia spreading along a lymph-vessel.

why a carcinoma should develop. The idea of congenital inclusion of tissues is not so applicable to cancer as to sarcoma. Wounds of various kinds are usually a coincidence rather than a cause. The influence of heredity is no longer considered more than predisposing. Analogies with certain conditions known to be due to parasites have occupied the mind of inves-

tigators for many years, and various forms of cell inclusion and degeneration have been regarded as the lower organism to whose entrance into the body the carcinoma is due. Transplantation experiments have succeeded in a very few cases and this apparent success has been taken as proof of the parasitic nature of carcinoma. But the spontaneous transplantation, by emboli, of a tumor situated elsewhere in the same body should not be forgotten, and the transplantation to another body may perhaps be explained as a piece of tissue rather than a germ finding conditions satisfactory for its growth. Fungi, bacteria, sporozoa, amebæ, gregarinæ, blastomycetes and coccidia have all been considered as the parasite, but none has been proved so far. Form and staining properties have been relied upon to demonstrate them, but cultivation and inoculation are required first before the matter can be decided. Granted that a parasite is demonstrated, the accessory and adjuvant influences, of which we know more at present, must still be considered in causation.

The whole course of the disease, however, does not correspond to any parasitic infection with which we are acquainted. There are no sudden increases in the number of cases with periods of declining frequency, and the apparent steady growth in the prevalence of cancer is to be explained partly as improved diagnosis and partly as the indirect result of improved public sanitation, more people reaching the age when cancer develops in proportion as the length of a generation is extended. Granted for the moment that some parasites may cause tumors, as coccidia in the liver and Bilharzia in the bladder lymphatics, the view of malignant cell proliferation as accelerated "habit of growth" refers parasites to the only importance which can be safely claimed, *i. e.*, one among many possible stimuli of such proliferation.

## F. Cysts and Teratomata.

Under the name cyst many forms of tumor are grouped, consisting of a cavity lined with epithelium or not, containing

more or less fluid material, serous, mucous, hemorrhagic, etc.; and also certain parasites occur in cyst form. The tumor is simple or divided into many smaller compartments, hence called multilocular, and the secondary cavities may be only in the wall of a large cyst; by breaking down septa a multilocular cyst becomes simplified into one large cavity, the wall marked by incomplete partitions which persist. Many cysts remain stationary as small tumors, some grow slowly but steadily and may reach an enormous size, degenerations in wall and contents are common. Strictly speaking the exclusion from the economy of a blood extravasation or a degenerated area by the formation of a fibrous capsule is not an example of a cyst, nor similar formation about a parasite or foreign body. Apart from such forms we distinguish cysts developing in a body cavity and cysts of new formation.

Cysts of the first variety are usually called retention cysts and occur when a gland lumen or duct is closed and its contents accumulate, as from pressure, foreign bodies, stenosis and other mechanical causes; the contents may be that of the gland involved or the same variously altered. These cysts are further divided into follicular, mucous, and those of large canals. An example of the first is found in comedo, sebaceous cysts (sebatoma) and of the Graafian follicle; examples of the second occur often as polypoid growths on mucous membranes; the third variety is observed in connection with large glands like the breast, the liver and the kidney. A special variety may be made of cysts developing in canals which normally disappear in the complete development of the body, as in the urachus, the parovarium, the hydatids of Morgagni, and the primitive branchial clefts.

Cysts of similar formation may be congenital and are divided into dermoid cysts and teratomata. They depend upon disturbances of development and dislocations of part of one or more embryonic layers. The dermoid cysts received their name from the resemblance between their walls and the normal skin, and

in simplest form they contain epithelial scales and the products of their degeneration, hair, subaceous glands and fat; or they may also contain teeth, imperfectly formed bone and mucous tissue. They occur in the subcutaneous tissue, connected with periosteum, in the orbit and the antrum.

Teratoma is the name applied to such tumors when they contain portions of a more or less imperfectly developed embryo, like a limb or a gland, and they are found especially often about either end of the main axis, connected with the pelvis or the head. Where the inclusion approaches in completion the child at term, the case is referred to the double monsters.

Cysts of new formation, proliferation cysts, belong to the true neoplasms. They increase by formation of new tissue, accumulation of their colloid or mucinous contents, and the degeneration and distention of new portions. They occur most often in the ovary, kidney, and testis, and are described as either glandular or papillary. (See Diseases of the Ovary, p. 570.)

# CHAPTER VIII.

## ANIMAL PARASITES.

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A PARASITE is an organism which lives in or upon another, and the most important are those which live at the expense of others. All degrees of parasitism are found, from simple co-existence and a common source of food (commensalism), to actual destruction of the host by the parasite. The subject has many sides, but from their disease-producing action certain kinds of vegetable and animal parasites require special mention; the vegetable comprise the fungi and the bacteria, and will be treated in Chapter IX.

The animal forms, for which the name parasite is reserved by common habit of speech, occur both on the surface of the body and internally. Some go through only a stage of their life history as parasites, some are wholly parasitic, others are optional parasites, able to live apart from man (as certain mosquitoes which live on vegetable juices in the absence of animals). As nutriment is obtained without much labor, the organs of a parasite may be variously aborted, the external kinds retaining locomotive or grasping organs, the internal at times having no digestive or respiratory systems, since they absorb both gas and nutriment from the tissue juices; hence they may retain only reproductive organs and if the sexes are separate one may be more rudimentary than the other. Their reproductive energy in some cases is enormous.

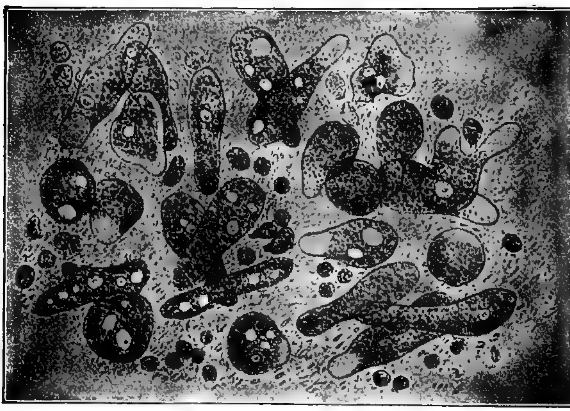
The effects of parasites may be either mechanical or chemical. Mechanical are: Stoppage of lumen of gut, vessel or gland ducts; pressure; bleeding from direct suction, perforation of vessels after inflammation. As chemical may be mentioned:

Poisoning the host, irritation and inflammation, local necrosis, and many reflex nervous symptoms.

## Protozoa.

**Rhizopoda.** 1. *Ameba coli.*—Occurs in intestinal contents, ulcers of gut, secondary abscess. Single spherical cell in quiet stages, puts out pseudopods when active, 15-25 $\mu$ in diameter, periphery hyaline, protoplasm finely granular; may contain red

FIG. 46.



AMEBA COLI. (*Stengel.*)

cells and bacteria; encysted form smaller and may show nucleus; found in great numbers in stools of tropical dysentery. Perforate mucous membrane of gut, cause necrosis, inflammation and secondary abscess of liver. Ameba coli is said by some authors to be innocent and ameba dysenteriæ, another form, the cause of injury cited.

**Sporozoa.** *Gregarinae; Coccidia.*—Cell parasites, widely distributed, spheroid or with one diameter much longer than others, covered by firm cuticle, make countless spores when encysted, which reach cells and develop, then become free in

gut and gland ducts; move but little or are very active; perhaps the best known form is the coccidium oviforme of rodents, of which the spores are called psorospermiæ. Another kind said to occur in molluscum contagiosum. Miescher's "tubes" (Sarcosporidia) are another instance of parasitic sporozoa; they occur in muscles and fascia of mouse, hog, elk and man (rarely) as falciform bodies, often calcified, strongly resembling trichinæ.

**Acystosporidia.**—Best known forms those of bilious typhoid, black-water fever, bird and human malaria and Texas fever of cattle (fam. Hemamebidæ).

*Malarial Plasmodium.*—Parasite, one-celled, one stage of its life in mosquito (anopheles) and by it inoculated upon man. In the body of man occurs as ameba with active motion, or as long crescents usually motionless except pulsation; both possess hyaline protoplasm and a diffuse or distributed nucleus.

Ameboid form; pale structureless disks in red blood cell; inclose pigment granules as they increase in size, show ameboid movement till large adult fully pigmented stage is reached, while red cell changes in shape, size and color. Reproductive stage follows, the ameba quiet; pigment collects at center, rarely periphery (presegmenting form), delicate radii appear splitting ameba into segmenting forms (rosette) commonly 18 in number, disposed about a dark unsegmented residuum. Corpuscle breaks and sets segments free as small roundish or oval spores each with a central refracting nucleus; these reënter red cells and repeat the cycle, which is thus equivalent to continuous self-inoculation of the host. Fever paroxysm and breaking up of rosette coincide. The second form of the organism which secures its existence outside of the human body (exogenous cycle) is produced by conjugation of a single flagellum of the "male" flagellate form with a large, pale non-ameboid "female." Three forms are recognized:

*Tertian Parasite.*—Life of each generation forty-eight hours, hence fever every second day; with two broods maturing alter-

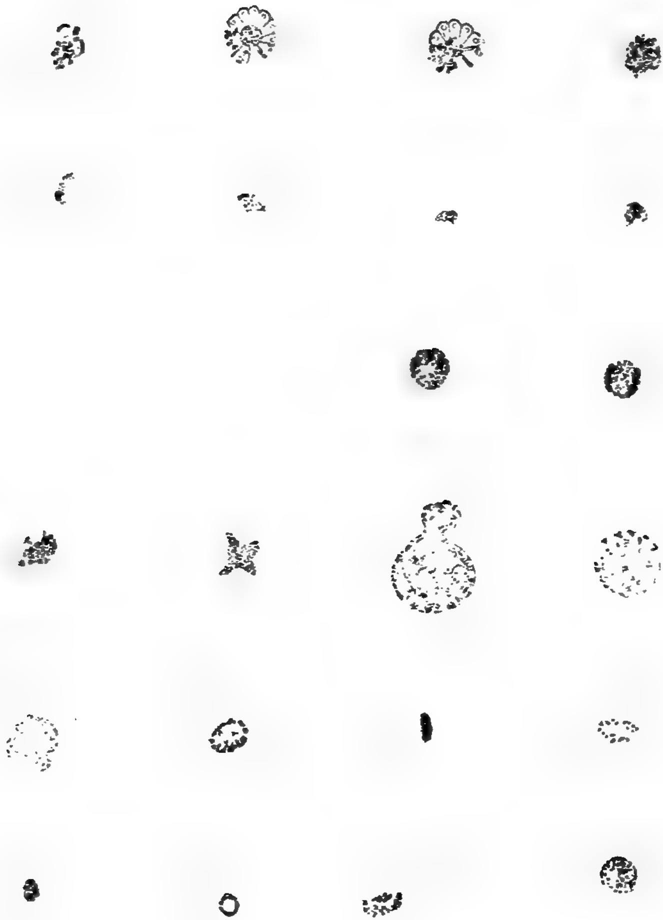
nately fever becomes quotidian; hence called double tertian by some authors. Adult pigmented form nearly or quite fills red cell, fifteen to twenty round or oval spores at a time set free from one red cell; this occurs in marrow and spleen or in peripheral circulation. Commonest type in temperate zone.

*Quartan Parasite.*—Broods mature every seventy-two hours, paroxysm of fever once in three days; with double or triple infection fever comes every two days, with a free one following, or every day. Ameboid stage refractile, clearly outlined, grows and moves slowly, no pseudopods found. Pigmented form contains few but larger granules, pigment darker, radiating lines more distinct, spores larger and fewer and nucleated, as are all malarial spores; red cell apt to be shrunken, not so decolorized. Segmentation in peripheral blood and internal organs.

*Estivo-autumnal Parasite.*—Fevers caused are irregular, quotidian, tertian or pernicious, the latter remittent or continuous. Cycle varies from twenty-four to forty-eight hours. In smallest form the ameba seldom reaches size of red cell (about 1/3) and cell may contain more than one. Young hyaline form is signet-ring-shaped with clear, non-staining center, may be found free in plasma; pigment absent or in small grains eccentrically placed; spores small, from six to thirty. Red cell shows no effect or shrinks, with coloring matter grouped about the parasite and rest of cell paler. Crescentic form appears after paroxysm as round, oval or spindle-shaped bodies one-fourth the diameter of the red cell (young form of crescent); grow to be 1½ diameters of red cell by one-fourth, and either spindles or crescents, homogeneous and highly refracting; pigment granules fine and grouped in mid-zone; red cell may persist as delicate line like bowstring from end to end of crescent. Flagellate forms develop outside red cells, flagella appear suddenly and by their activity move the parasite or cause adjacent cells to move

Outside the body of man they exist in the stomach of anopheles as either hyaline or granular forms, the latter not flagellate; undergo changes in mosquito stomach for about 8-10 days

FIG. 47.



ILLUSTRATING DIFFERENT FORMS OF THE MALARIAL ORGANISMS WITH THEIR STAGES OF DEVELOPMENT. (*From Tyson's "Practice of Medicine."*)

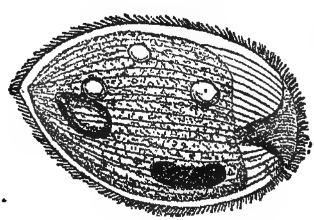
$A_1$, $A_2$, $A_3$, $A_4$, sporulation stage; $B_1$, $B_2$, sporules separating; $C_1$, $C_2$, free sporules; $D_1$, $D_2$, epi-corpuscular forms; $E_1$, $E_2$, $E_3$, $E_4$, intra-corpuscular forms; $F_1$, $F_2$, the large extra-corpuscular body; $G_1$, $G_2$, the flagellate forms; $H_1$, $H_2$, $H_3$, $H_4$, $H_5$, $H_6$, the crescent-shaped parasite and its developmental

and small filiform bodies then found in poison glands of host; from there introduced at time of stinging human body. See p. 207.

CHIEF DIFFERENCES BETWEEN THE PARASITES.

| TERTIAN. | QUARTAN. | ESTIVO-AUTUMNAL. |
|---|---|---|
| Cycle in man 48 hours, | 3 days, | 24-48 hours. |
| Ameba in red cell active, | sluggish, | smaller than tertian. |
| Decolorizes red cell rapidly, | slowly, | hemoglobin deeper in tint. |
| Causes red cell to swell, | size preserved or diminished, | red cells shrivel. |
| Outlines not sharply defined, | sharp, | |
| Pigment in fine granules abundant, in motion, | coarser, fewer, | pigment in fine peripheral granules, not often in motion. |
| Spores 15-20, usually 18, small, | 6,12, larger, | small, 6-30, usually 18. |
| Flagella more numerous, | | less numerous. |
| Ring-forms common, early, more distinct than those of estivo-autumnal, | | common, ring and disk forms less distinct. |

FIG 48.



PARAMECIUM COLI. (*Delafield and Prudden.*)

**Infusoria.**—Bodily structure more complicated, consisting of ectosarc, sometimes striate, and endosarc, granular; present rudimentary intestinal canal with differentiated openings which lead directly into the protoplasm; may have a pulsating vacuole which is both circulatory and excretory in function; surface covered with cilia; reproduction by fission or conjunction of two. Divided into flagellata, ciliata and suctoria.

*Ciliata.*—Most important are (1) cercomonas intestinalis, pear-shaped, transparent, 8-10 $\mu$ in length, with short blunt tail and long delicate cilium which thrashes in medium and produces locomotion; found in feces of diarrhea, cholera and typhoid; (2) trichomonas vaginalis, oval, 15-25 $\mu$ long, single cilium at one end and bundle of cilia at other, undulating membrane on the side; found in urine, vaginal secretion and sputum; and lastly, (3) paramecium coli, ovoid, .06-.1 mm. long, one or two contractile vacuoles, surface covered with cilia; found in diarrheal feces and sputa from abscess of lung.

**Vermes.**—Animals in segments usually, with laterally symmetrical cylindric or flattened bodies, without appendages except bristles or clinging apparatus; internal organs complicated, at times blood, nervous and digestive systems present, or one or all may be lacking; sexes separate or coexist; most important parasites of man and other vertebrates. Chiefly occur as flat and as round worms:

Flat worms (Platyhelminths).—

Cestodes—Tapeworms:

Tenia solium and mediocanellata,
Echinococcus.
Tenia nana and cucumerina,
Bothriocephalus latus.

Trematodes—Sucking worms.—

Distomum hepaticum, lanceolatum, hematobium.

Round worms (Nemathelminths).—

Acanthocephali:

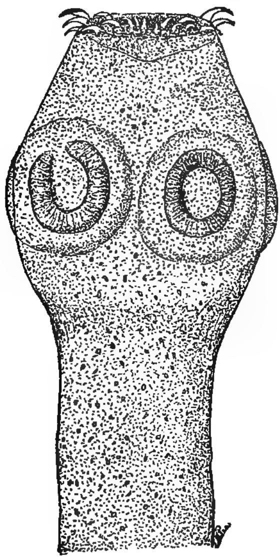
Echinorhyncus hominis.

Nematodes:

Ascaris lumbricoides, mystax,
Oxyuris vermicularis,
Eustrongylus, Strongylus, Dochmius,
Anguillula stercoralis,
Trichocephalus dispar, Trichina spiralis,
Filaria medinensis, Filaria sanguinis hominis.

The flat worms have either segmented (Cestodes) or unsegmented (Trematodes) bodies, flat and tongue- or leaf-shape, a branched excretory system, intestine absent in Cestodes, present in Trematodes, external prehension apparatus as hooks, sucking disks, etc., hermaphrodite.

FIG. 49.



HEAD OF TENIA SOLIUM. (*Delafield and Prudden.*)

**Cestodes, Tapeworms.**—Without mouth or gut, consist of a head (scolex) and segments (proglottides), the latter rectangular and increasing in size with the distance from the head, the largest end segments breaking off and passing out of the host in the feces; eggs are produced in the larger segments. On plants, in water or manure, remain for a time and then swallowed with the food of another animal, the egg coverings digested off and embryos set free. They bore into the tissues

or vessels of the host and develop in various organs to bladder-like larvæ, from whose walls new sexless individuals form. These passively gain entrance to a new host (through use of animal food) and develop to a new colony of segments.

*Tenia solium.*—Frequent in man, several meters long, coiled in the gut or stretched, may be several present, head 1 mm., segments 10 mm. by 6 mm., head furnished with a rostellum and 26 hooklets, behind which are four sucking disks; eggs ovoid, about 35 μ long, embryo occurs as measles in pork and as cysticercus cellulosæ in muscles, brain and eye of man. Occurs specially in cooks, butchers, and those who eat imperfectly cooked pig meat. The worm develops quickly in the lower part of the small intestine, may reach a length of 2-3 meters in as many months, and may persist 10 years.

*Tenia mediocanellata* (*saginata*).—May be 6 meters long, head 2.5 mm. broad, no hooks or rostellum, four strong disks usually surrounded with line of pigment, segmentation in the neck evident to the naked eye, uterus has many side branches which divide dichotomously; grows as a whole about 12 segments a day; eggs more oval than T. solium, with a thick shell and lining membrane; proglottides passed singly; common, usually single, follows use of uncooked infected beef.

*Tenia echinococcus.*—Occurs in domestic animals as a small, trisegmented worm, about 4-5 mm. long, rostellum conical, 28-46 hooklets in two rows; last segment has a branched uterus, irregular, full of long oval eggs. Larvæ gain entrance to human intestine, wander into various tissues, especially the liver, and slowly develop into cysts with a wall in many layers. After five months the daughter cysts develop from the inner wall of this, projecting into the fluid contents of the main cysts (echinococcus hominis, endogena) or more rarely project outwardly (e. scolicipariens, exogena). Cyst contents clear, free from albumin; may reach an enormous size, may degenerate by absorption of fluid and fatty changes. From the dog as only known source. Clinical importance of such cysts according to size and

location; found in liver, lung, peritoneum, skin, muscles, kidney, spleen and brain. Most common in Iceland.

*Bothriocephalus latus.*—Largest human tapeworm, may be 8 meters long (3-4 thousand segments), head looks like a swelling of the thin neck, marked by two deep sucking furrows arranged longitudinally, segments 10-12 mm. broad by 5-8 mm. long, passed in groups; uterus a simple canal variously bent from side to side in the middle of a ripe segment; eggs oval, brownish, develop in fresh water to a ciliated, freely moving sphere; occur especially in Switzerland in certain fish (as the pike), and by their use as food in human beings also.

**Trematodes, Sucking Worms.**—These parasites as found in human beings are members of the family Distomidæ, internal parasites with a sucking organ at the oral aperture and another on the abdominal aspect, the intestine is forked and ends blindly, the uterus contains oval eggs which even in the parent develop into ciliated embryos; divided into two groups, the distoma with hinder sucker in the cephalic half, and amphistoma with the second sucker at the posterior extremity.

*Distomum hepaticum.*—Shaped like a flat high-shouldered bottle, 15-40 mm. long by 12 broad, tapers more sharply backward, both suckers small and near together at the head end, between them the genital pore; hermaphrodite, the pore serving as common duct for both sets of organs, often presents a thick spiral cirrhus (penis), multiplies by junction of two, each acting as both male and female; eggs oval, 0.13 mm. long. Worm occurs in liver, in gall-ducts and bladder, usually few at a time in man, causing inflammation of gall-passages; may penetrate vessels and be carried elsewhere.

*Distomum hematobium.*—Body longer, flat in male, more cylindrical in female, suckers at head end and close together, color white; male 12-14 mm. long, female 16-19 mm., eggs 0.12 mm. long, oval and somewhat pointed at poles; occurs in ureters, bladder and colon and causes inflammation (dysentery, pyelitis),

found in Egypt specially. Embryos develop in water and may have a mosquito or a crustacean as temporary host.

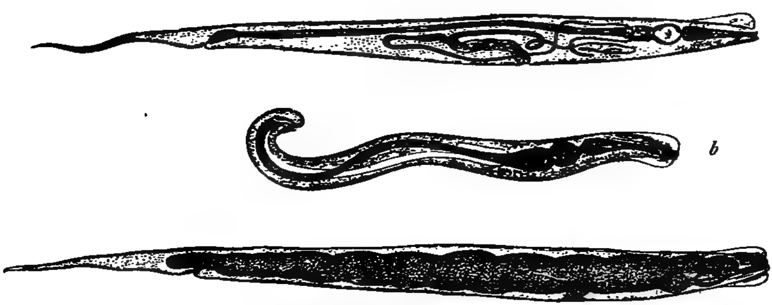
**Round worms (Nemathelminthes)**, of small or large cylindrical form, ringed but not segmented, sometimes with hooks or papillæ at the anterior end, blood and breathing organs absent, sexes separate.

**Acanthocephali.**—Only member of this order is the Echinorhynchus hominis, 5-6 meters long, with 12 cross rows of hooks, 8 in each row; very uncommon.

## Nematodes.

*Ascaris lumbricoides.*—Commonest intestinal parasite in man, cylindrical body tapering toward each end, four longitudinal

FIG. 50.




OXYURIS VERMICULARIS. (*Birch-Hirschfeld.*)

*a*, mature unfertilized female; *b*, male; *c*, female after impregnation, the enlarged ovary concealing other organs.

stripes and many cross ones; male 250 mm. long by 3 mm. thick, female 400 mm. long by 5.5 mm. thick, color pale red, head slightly different in color, intestinal canal runs through the entire worm to a vent on the hinder abdominal surface; tail end of the female somewhat blunt, double uterus, thread-like and twisted, may contain as many as sixty million eggs; these

are oval, with a thick shell, about 0.05 mm. long, covered by a layer of albuminous matter which preserves them for a long time after extrusion; may be no intermediate host, the eggs swallowed and immediately developed in human intestine; occur singly or in countless numbers; produce catarrhal inflammation of the gut, obscure nervous symptoms, perforation and abscess, or stoppage of various lumina, as gall-ducts.

*Oxyuris vermicularis; Thread worm, Seat worm.*—Small white thread-like worms, male about 3-4 mm. long, female 8-12 mm. long, tail of former rolled up, tail of latter very tapering, mouth end provided with three lips in each; genital pore posterior in male, anterior in female; intestinal canal straight and in the midline; eggs oval, 0.05 mm. long and contain an embryo with sharp posterior end. One of the common human parasites, in adults as well as children, chiefly in colon and about rectum and anus, from here may enter the vagina; produces catarrhal inflammation, nervous symptoms, great itching about anus; may be transmitted from use of common privies or the eggs may be dried and gain entrance by swallowing.

*Eustrongylus gigas, Palisade Worm.*—Uncommon, found in the renal pelvis at times, female 1 meter long by 8-12 mm. thick, male 0.5 meter, red color, male has bell-shaped copulatory bursa posteriorly, six papillæ about mouth, no pharyngeal dilatation.

*Strongylus.*—A small worm of this group has been found occasionally in the lung or the duodenum; gray white in color, mouth small with two papillæ on neck, bursa shallow, cupped.

*Dochmius.*—Mouth wide, furnished with teeth, lips hard, two claw-shaped hooks on ventral side of mouth, two smaller ones on dorsal edge.

*Dochmius duodenalis, Anchylostomum duodenale.*—Male 10 mm. long by 1 mm. thick, female 12-18 mm. long, body cylindrical; head bends towards dorsal aspect and furnished with a horny mouth capsule with two teeth ventral and one dorsal, gut large and often blood-filled, hind end of female pointed, of male arranged as a three-leaved cup; eggs oval with thin shell, about

0.04 mm. long; parasitic in upper part of small intestine where it clings to the mucous membrane and sucks blood for its nourishment, often in numbers; on separation from gut wall a small ecchymosis is left with a pin-point bleeding hole in the middle: if present in great numbers may cause a serious anemia, which may be fatal or lead to other disease. Occurs frequently in Egypt and Brazil, and a special form is common throughout sandy districts of the South Atlantic and Gulf States of the United States. The disease is called uncinariasis, hook worm disease, miners' anemia, etc.

*Anguillula stercoralis.*—Uncommon except in China, occurs in gut as extremely fine thread, 0.25 meter long, causes diarrhea, dysentery, anemia and emaciation.

FIG. 51.

TRICHOCEPHALUS DISPAR. (*Birch-Hirschfeld.*)

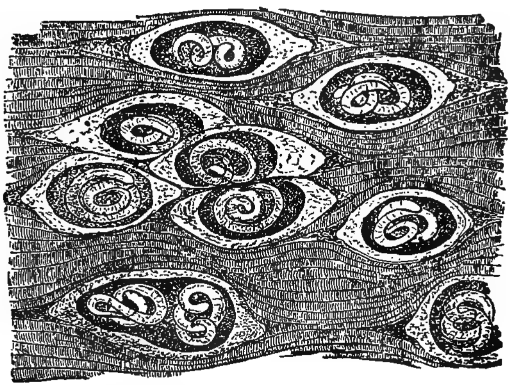
Natural size. *a*, female; *b*, male.

*Trichocephalus dispar.*—About 4 cm. long, anterior end long and very thin, small mouth without papillæ, occurs singly or in numbers in cecum and ascending colon, may pierce the gut wall if continuity broken by ulceration, otherwise appears to cause but little trouble.

*Trichina spiralis.*—In two forms in man and animals, as developed worms in the intestine, and as encapsulated in the muscular tissues; among animals most common in hogs, found also in rat, fox, bear, cat, and other carnivorous or omnivorous animals. Intestinal form thread-like with thinner head end and

round tail end, male 1.5 mm. long, female 2-4 mm. long; intestinal canal divided into pharynx, stomach, gut, and ends in a cloaca with the genital apparatus; eggs 20 $\mu$ in diameter, pierced by embryo while still in uterus and brought forth alive after 5-7 days in the stomach of host. This process may last several days with a total of 1,500-2,000 young worms, which bore through the walls of the alimentary canal and find their way to the voluntary muscles, the exact road travelled being still a matter of dispute, either passively by the blood stream, or ac-

FIG. 52.



TRICHINA SPIRALIS. (*Ziegler.*)

tively by way of the connective tissues and lymph channels; probably passive manner far more important. After the brood is hatched the female dies and is passed in the feces; the male usually has disappeared earlier. As early as two weeks after infection the worm may be found in the striated muscle within the fibers, where granular degeneration of the contractile substance occurs; then the worm rolls into a coil and lies in a lemon-shaped capsule which gradually becomes infiltrated with lime salts (6-18 months), showing as a small white point to the

naked eye. Thus encapsuled the worm may remain as long as 18 years, capable of development as soon as it reaches a stomach whose gastric juice can dissolve the capsule and free it; but it may also die and be absorbed; after the death of the host the worm withstands the process of decomposition for weeks. Occurrence in man depends greatly upon methods of preparing meat (pig) for the table; where properly cooked the danger

FIG. 53.

INTESTINAL FORM OF TRICHINA WITH EMBRYOS. (*Birch-Hirschfeld.*)
Only the middle portion of the worm shown.

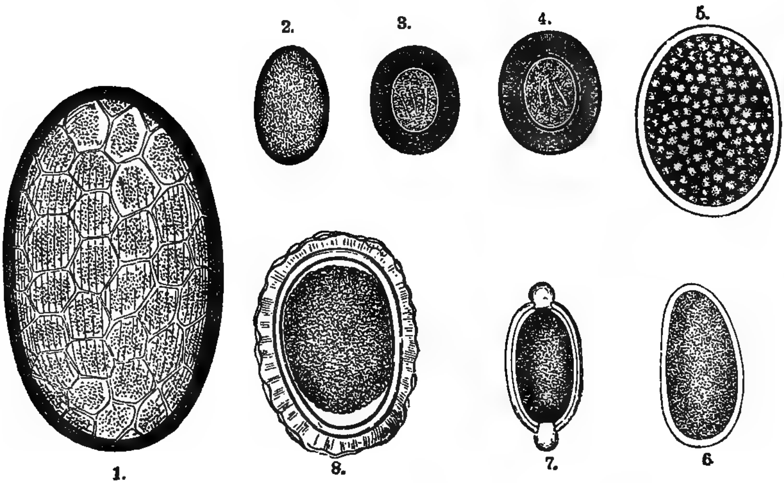
of infection is small as a temperature of 65° C., at which point the meat changes from a red to a gray color, destroys the worms; long pickling and smoking destroy the worms in the superficial parts of the meat but the central parts may still contain live ones.

*Filaria medinensis, Guinea Worm.*—Female 1 meter long by 2 mm. thick, circular oral aperture with four hooklets, tail

pointed; uterus fills the greater part of the body and contains countless embryos with pointed tails; occurs in the tropics in the subcutaneous tissues, especially of feet and legs, causing bleeding and inflammation; embryos live free in fresh water and occur in crustacea as intermediate host.

*Filaria sanguinis hominis.*—Embryos occur in the blood of

FIG. 54.




EGGS OF VARIOUS INTESTINAL WORMS. (*Birch-Hirschfeld.*)

1, distomum hepaticum; 2, distomum lanceolatum; 3, tenia solium; 4, tenia mediocanellata; 5, bothriocephalus latus; 6, oxyuris vermicularis; 7, trichocephalus dispar; 8, ascaris lumbricoides.

patients in tropical countries causing hematuria and chyluria, 0.35-1 mm. long by 0.006 mm. broad, head blunt, tail tapering; one drop of blood may contain 6-12, appearing periodically (as at night alone); extruded through the kidney where they cause bleeding and loss of lymph. The developed worm occurs in the subcutaneous tissues and causes lymphangitic elephantiasis, as of scrotum and legs. Common in Egypt, India and China; in-

termediate host probably a mosquito, set free in water by the death of the same and so carried to man.

**Arachnoidea; Insecta.**— External parasites are chiefly members of the spiders or insects which cause inflammation of the integument by boring and biting, and are usually only an inconvenience. Most important for man are such forms as act the part of intermediate host for some internal parasite, and particularly the fly, which mechanically carries typhoid bacilli from feces to the food of man and so spreads the disease, and the mosquito, which in some of its forms carries filaria sanguinis hominis, the bacillus of tetanus, the plasmodium of malaria and the unknown agent which produces yellow fever. The plague is propagated indirectly by ants, mice and rats, as typhoid by flies.

The malaria-carrying mosquito is proved to be one of the genus Anopheles (especially A. quadrimaculatus or claviger and A. punctipennis, though probably others also). Texas fever, bovine malaria, is carried by a tick (boöphilus bovis); a similar disease of birds by culex pipiens. In non-malarial countries only Culex occurs, in malarial the genus Anopheles also. This genus is described as follows: Palpi in both sexes about as long as the proboscis, 4-jointed in female, 3-jointed in male, though a constricted basal joint seems to add another to each; palpi straight filaments and in female held parallel with proboscis except when biting, then raised and divergent; nucha has posterior scaly cornu, abdomen pilose on both surfaces, not scaly; legs long and end in simple ungues or dentate claws; wings often spotted, and magnifying glass shows spots made up of black squamæ on brownish wing; length, including proboscis, female 7.5-9 mm., male smaller and does not sting; resting on perpendicular surface, as a wall, Anopheles stands with main axis at right angles except when heavy with blood, Culex holds body parallel.

Cycle within mosquito — a flagellum (or microgamete) of the flagellate organism unites with ameboid (macrogamete),

the former the "male," the latter the "female"; then the fertilized ameba develops between the muscle fibers of the mosquito's mid-intestine, takes on capsule and becomes sporozoon. Its nucleus divides and subdivides to form sporozoites, very slender filaments with curved ends and in middle a nucleus, with a little chromatin in rods and bundles. The capsule breaks, sporozoites distribute through body and gather especially in salivary gland, thence inoculated at time of stinging: the cycle takes 8 to 10 days. As the form in the mosquito is more highly organized than the forms in man, he is the intermediate host for the insect's parasite.

Stegomyia fasciata is the mosquito which carries the infection of yellow fever. It flies chiefly in the day time, and is very insidious and persistent in its attack. In 3-6 days after taking blood, the female lays her eggs. When contaminated with the yellow fever organism, for which the name myxococcidium stegomyiæ has been proposed, the eggs degenerate before oviposition.

The female: 3.5--5 mm. long, head clothed with flat scales, black and gray on each side, white patch in middle, in front, reaching back to neck, a white patch on each side, and thin white borders to eyes; antennæ blackish with narrow pale bands; last joint of palpi white on inner side. Thorax dark brown, ornamented with white curved band on each side of back and white spot on each side in front. Abdomen dark with basal bands of white. Fore and mid ungues toothed, hind ones not.

Eggs, 40--150 in single brood, of black color, float in water, hatch in 10--24 hours. Entire metamorphosis of insect complete in 8--10 days.

About three days after feeding on yellow fever patient the fusiform protozoa of the parasite can be seen in the stomach of the insect. The sporoblasts (?) enter the salivary glands and break up into sporozoites; these infinitesimally small

bodies pass out of the lumen of the gland when the insect feeds again.

The best stains for serial sections of the mosquito are iron hematoxylin (Heidenhain's), and saturated solution of Bismarck brown in hot 60 % alcohol.

After an infected mosquito has bitten a person who is not immune he may develop yellow fever. Blood taken from a case of yellow fever during the first or second day will give the disease when injected into the circulation of a non-immune. An attack from the bite of the mosquito makes one immune against such injection.

Other external parasites, as itch insects, ticks, lice, etc., cause skin lesions which may be studied in any standard work on dermatology.

# CHAPTER IX.

## VEGETABLE PARASITES.

UNDER the head of microörganisms are grouped:

Saccharomycetes or Yeast fungi,
Hyphomycetes or Mould fungi.
Schizomycetes or Fission fungi.

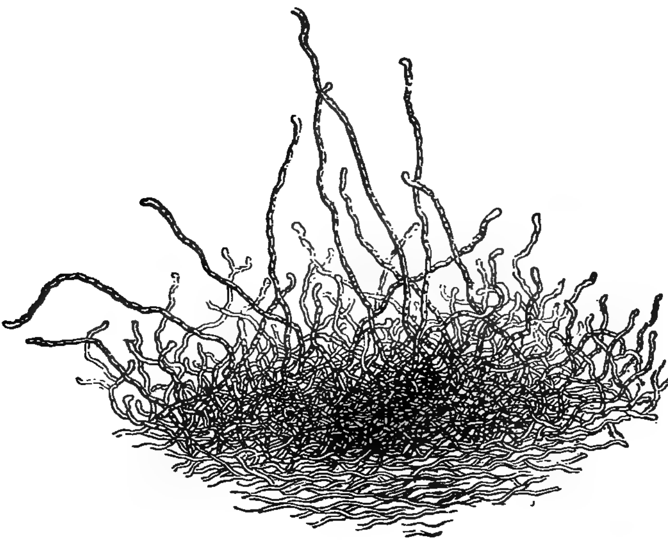
These all belong to the lowest plants, the non-chlorophyll-forming thallophytes, and are parasitic both upon and within the body of man, animals and other plants, but so far as man is concerned the latter (schizomycetes) are by far the most important because of their frequent causation of disease and consequent relation to hygiene and preventive medicine. They all derive their nutriment from more complex compounds of carbon, and if from dead organic substances they are called saprophytes, if from living tissues, parasites; both occur in man.

Yeast fungi occur as harmless saprophytes in man, naked or encapsuled cells of round or oval form, and are constant in the alimentary canal, especially in the mouth and stomach; if found in the bladder which contains urine and dextrose, fermentation may occur with gas formation. Certain species may occasion suppurative inflammation of the various tissues but very rarely. The cells multiply by budding and the bud after reaching a certain size is constricted off; when nutritive material is scant they may form sterile threads.

Mould fungi play an important part in certain superficial disorders of skin and mucous membranes. They occur as threads

(hyphæ) woven together into a tangle (mycelium) from which certain filaments rise bearing short cylindrical or round cells, the spores, grouped or singly. Though growing on the skin, in the hair, on the mucous membrane of mouth and vagina, they do not live on cells of good vitality but on those dying or dead; less often they appear in more central parts, for the temperature

FIG. 55.



OIDIUM ALBICANS OR THRUSH FUNGUS. (*Birch-Hirschfeld.*)

Growth from mucous membrane.

is too high and the oxygen supply too low. A common form is the fungus of thrush, or aphthæ (Oïdium albicans) which may occur in the normal mouth without symptoms but in the debilitated may grow at the expense of the tissues.

Thread fungi produce various skin diseases, as favus, pityriasis versicolor, herpes tonsurans, etc.

Microsporon furfur, fungus of pityriasis versicolor; delicate threads in the outer layer of the skin of the breast and back, causing peculiar branny and brownish spots from simple points to several centimeters wide; in scrapings a mycelium of thin branching threads, 1-2 $\mu$ broad, empty or filled with spores; between the threads lie spherical groups of spores.

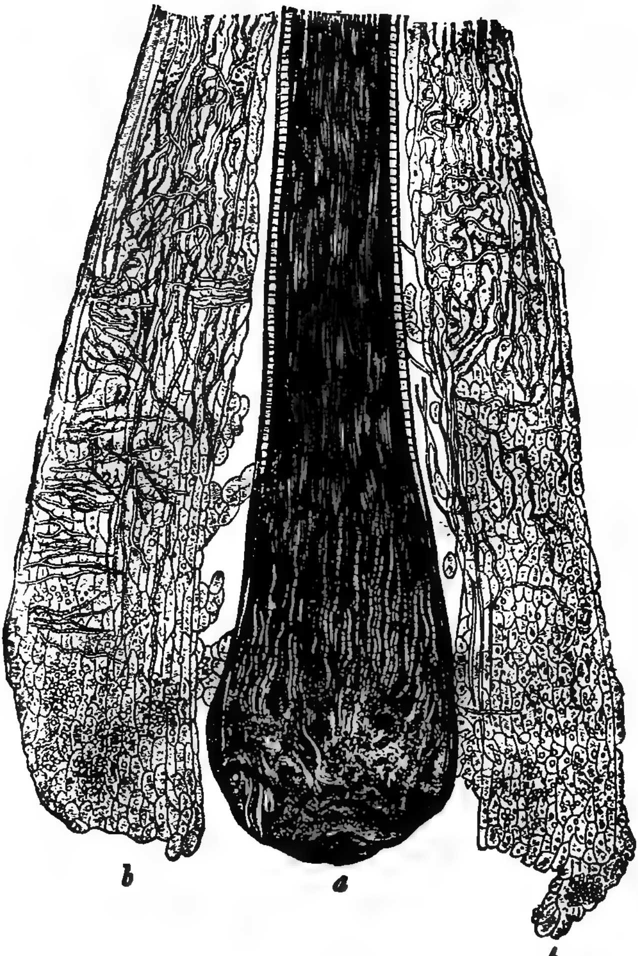
Microsporon minutissimum occurs occasionally in the skin in parts usually covered, causing brownish patches but little scaly; resembles M. furfur, but is more delicate.

Trichophyton tonsurans occurs on hairy parts (scalp) affected with herpes tonsurans, causing partly bald, round spots, of grayish color and covered with moist or dusty material, presenting broken hairs here and there. The dust is made of dried epithelia and fungus spores, which are more numerous than the mycelium and fill the hairs from root to outer end, 0.004-0.01 mm. in diameter, often arranged in chains; free ends of hyphæ rounded. In sycosis parasitica and eczema marginatum a fungus is found which is said to be identical with that of herpes tonsurans, as also perhaps with that of ringworm.

*Achorion Schoenleinii.*—This fungus, the cause of favus, is found as continuous or segmented hyphæ with branches at right angles, homogeneous or granular, ends somewhat pointed, mycelium more numerous than spores, which are long oval in shape, 0.005-0.008 mm. in diameter: develops in the hair-follicles, surrounds the bulb and pierces the hair, growing throughout its different layers. In the gross there are round, yellowish plates each about 10 mm. broad, pierced by a broken hair, easily lifted from its bed and hiding below it a drop of thick yellow fluid, these join and make large thick crusts of an unpleasant mouse-like odor. This fungus is passed from one patient to another readily and may invade hairless parts, as the nails and even the lung and intestine.

In general the fungi are more frequently pathogenic for lower animals than for man.

FIG. 56.




HAIR WITH FAVUS. (*Kaposi.*)

*a*, hair infiltrated by mycelial threads showing few spores; *b*, its sheath, showing many spores.

## Schizomycetes: Fission Fungi.

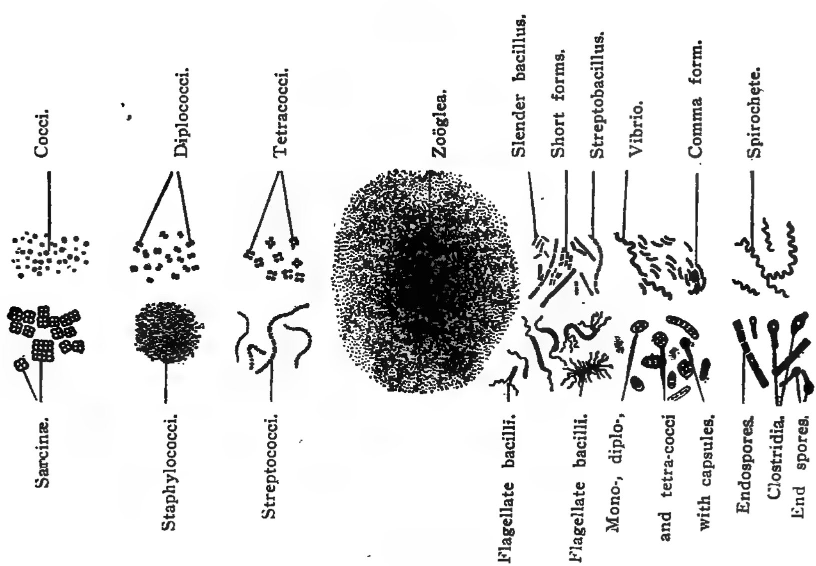
Three chief morphological groups of bacteria are usually described:

1. Coccus or spherical, single or in groups; if two occur together, diplococcus; if four, tetracoccus, meris-
2. Bacillus, rod-shaped, in twos, diplobacillus; in chains, streptococcus; if in bunches like grapes, staphylococcus; irregular masses, zoöglea.
2. Bacillus, rod-haped; in two's diplobacillus; in chains, streptobacillus; certain long forms are called leptothrix; spindle shapes, clostridium.
3. Spirillum, comprising the vibrio, short, bent like a comma, with a single end-flagellum, sometimes arranged in series; the true spirillum, long, spirally twisted and rigid, usually with polar flagella; and the spirochete, long, slender, spiral, pliant, without flagella.
4. Pleomorphous forms:
   (*a*) Cocci and short rods which develop to long threads forming arthrospores (proteus).
   (*b*) Filiform bacteria with no distinction between the ends, non-branching (leptothrix).
   (*c*) Filiform with ends differentiated, branching (cladothrix).

*Biology of Microörganisms.*—Bacteria or germs are composed of plasma (mycoprotein) enclosed in a membrane; in addition some forms have a capsule. Cocci are non-motile, in the other groups many kinds move actively, owing to the possession of flagella, thread-like processes capable of thrashing movement, some have but one, others many. Multiplication occurs by transverse division and is very rapid in good nutritive media. When the supply of nutriment is beginning to fail and sometimes otherwise, many bacteria show a second manner of prop-

agation, by spores, which are formed inside the sheath of the germ (endo-spores), either in the middle or at one or both ends, or separated off from the end (arthrospores). Spores are found more abundantly in the dark than in the light, and in red or yellow light than in white or violet. Multiplying by fission, if they remain in linear series and attached they form streptococci

FIG. 57.




THE FORMS OF BACTERIA. (*Coplin.*) Magnified 700 times.

and streptobacilli; if irregularly heaped together the condition is expressed by staphylo- and is found only in the cocci; massed and surrounded by a mucilaginous common envelope the term zoöglea is applicable. With the loss of nutrition various distorted involution forms occur.

*Chief Forms and Sources of Nutriment.*—Preformed organic matter soluble in water, water itself in plenty, potassium, sul-

phur, calcium, magnesium, etc. Carbon may be obtained by bacteria from soluble carbohydrates, weak alcohol, carbolic acid and other chemicals which in strong solution would destroy them; nitrogen from albumins, amines, amides, nitrates and ammonia; sulphur from various salts of sulphuric acid. The relation to oxygen is important:

Microörganisms requiring oxygen are called aërobic;
" able to grow in it, facultative " ;
" unable to grow in it, anerobic;
" able to grow without it, facultative anerobic.

In general the anerobics all form gas, liquefy gelatine, have a strong odor, are motile, and have spores.

Carbon dioxide restrains the growth of some germs (proteus) but is without influence on others (typhoid bacillus).

Sunlight by its blue, violet and actinic rays will destroy even the most virulent in the presence of oxygen, owing to the formation of $H_2O_2$.

Temperature is of the greatest importance, each variety having its point of best growth (temperature optimum) and exhibiting less activity as the heat varies from this. But even in the cold produced by liquid air many forms are not destroyed, growth reappearing when the temperature is raised; and at higher ranges of heat than the optimum a culture may merely lose some of its vigor. The highest point reached is about 65-70° C., at which level the bac. thermophilus will flourish, but as a rule 50-60° C. gradually weakens and then destroys almost every form. The spores show more resistance to heat, as to other influences, for while boiling water and steam at 100° C. will kill all bacteria, certain spores will endure this extreme for a time, and in the absence of moisture a temperature of 140° C. may be necessary to kill them. Temperature optimum and pathogenic powers for man stand in close relation, those bacteria which cause disease being varieties which grow between 10° C. and 45°C., with optimum about 37°, the body temperature. Grouped according to temperature:

Bacteria growing between 0° C. and 30° C. are psychrophile,
Bacteria growing between 10° C. and 45° C. are mesophile,
Bacteria growing between 40° C. and 70° C. are thermophile.

Drying stops multiplication and then destroys most bacteria, sometimes being preceded by spore formation and the spores persisting indefinitely. Many chemical substances, including the products of the bacteria themselves, restrain or destroy them; as used in medicine such chemicals are called antiseptics and for most purposes are sufficient if they only prevent multiplication and active growth. Of these chlorine, bromine, carbolic acid, potassium permanganate, mercuric chloride, and formaldehyde are the commonest.

(See table of antiseptics, p. 330.)

Different kinds of bacteria in the same medium may assist each other's growth (symbiosis) or overwhelm each other.

Certain bacteria form various pigments (bac. prodigiosus and pyocyaneus), others are phosphorescent, others form acids and various kinds of ferments, and these special properties depend closely upon the conditions of best growth, being lost for a time when nutrition, etc., fail; but of all bacterial products those poisonous to human tissues are most important here. By their activity in splitting higher chemical compounds into more simple, bacteria form several kinds of products, as:

A. Proteins: called pyogenic if causing suppuration, pyrogenic causing fever, phlogogenic causing inflammation. The protein of glanders (mallein) and of tuberculosis when injected into man or animal suffering from these diseases will cause a marked rise of temperature; used chiefly for diagnosis in veterinary practice.

B. Ferments: these are assumed to exist from certain effects which they explain, act apart from the bacteria producing them (as in filtered cultures) and resist antiseptics; splitting up carbohydrates is called fermentation, similar action on albumins is called putrefaction, the ferments, enzymes.

Chief ferments: acting on

Proteids, dissolving them in alkaline medium, like trypsin;

Milk, coagulating it and dissolving the curd, like pepsin;

Fat, forming glycerin and fatty acids, like steapsin;

Sugar, inverting it;

Starch, forming sugar, like ptyalin;

Urea, forming ammonium carbonate.

C. Other products of great variety, as

1. Acids; acetic, butyric, formic, lactic;
2. Aromatic substances; indol, phenol, skatol;
3. Derivatives of proteid digestion, albumose, peptone;
4. Gases, $CO_2$, $H_2S$, $PH_5$, $NH_4$;
5. Nitrogen compounds; amins, leucin, tyrosin;
6. Ptomains;
7. Toxins.

*Ptomains and Toxins.*—A ptomain is a basic subtance, contains nitrogen, is found in putrefaction of proteid matter, and resembles alkaloids in its action, combining with acids to form salts; at one time considered the essential element in bacterial intoxication. Toxins are formed by most all pathogenic bacteria, both by analysis and synthesis, in the living organism; do not act like basic bodies, cause symptoms like animal and plant alkaloids (snake venom, abrin, strychnin), and vary with the source, each kind of bacteria having its own specific toxin; their effect on the human organism is immense in minutest dosage, not only constitutionally but also locally to less degree. The power of the organism to resist is shown in the time of incubation necessary for the elaboration of sufficient poison after the entrance of the germs; the percentage rises up to the limit of the emunctories to eliminate and the tissues to oxidize it, causing only indefinite symptoms of malaise, but just beyond this limit occur the symptoms of general poisoning, chills, fever, vomiting, etc. Toxins were thought to be albuminous in nature

and called toxalbumins, but now they appear allied rather to peptones. They are destroyed by exposure to sunlight, heating at 60-80° C., and the gastric juice; to cause symptoms they must appear in the blood (1/275 of a grain of tetanus toxin is fatal to an adult); they seem to have selective actions on certain cells.

*Taxis.*—Bacteria show three kinds of taxis, those to which they are suceptible and that which they cause; thus

Phototaxis is exhibited by many forms, for they arrange themselves especially in the red rays when exposed to a spectrum. All the other rays are bactericidal, especially the violet and ultra-violet.

Chemotaxis is the response to chemicals; positive, if the bacteria are attracted (aërobics by oxygen, typhoid by potato juice); negative, if repelled.

Cytotaxis is the power of the bacterium to attract certain cells; tubercle bacilli are negatively cytotactic for pus cells (polymorphonuclear leucocytes), but positive for lymphoid cells.

*Staining Reaction.*—Many bacteria have special affinities for certain anilin stains and certain staining methods are of value in identifying them because of this relation; see Gram's method, p. 320.

## Pathogenic Cocci.

**Micrococcus (Staphylococcus) pyogenes aureus.**—Found everywhere, especially in pus; spherical, 0.8 μ diameter, singly, pairs or groups, not motile, facultative anerobe.

*Culture.*—Gelatine. In stick grows as fine white line along puncture, develops yellow to golden color by third day, liquefies the medium and falls as yellow precipitate. Agar.—Opaque irregular white or yellow film, becomes more golden, clouds the agar, but does not liquefy. On plates, potato and serum grows freely. T. 30-37° C.

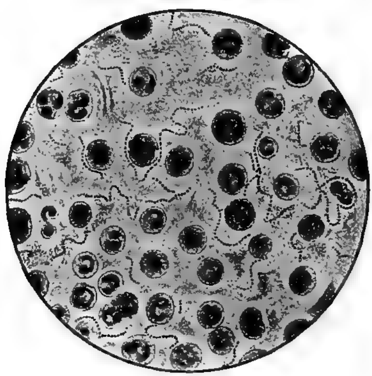
*Pathology.*—Injected into skin causes abscess; in the veins, multiple embolic abscesses, with fever, etc. (pyemia).

*Stains* with usual methods; G. +.[1]

**M. pyogenes albus** is like the above, except in producing no pigment, forming a white film on media; m. pyog. citreus produces a lemon-yellow pigment.

**Micrococcus pyogenes tenuis.**—Found in certain suppurations, not motile, singly and grouped, 0.9-1.0 $\mu$ diameter, aërobic. Grows as small transparent circles or streaks, gelatine and agar. Causes no symptoms in animals; stains with usual dyes.

FIG. 58.



STREPTOCOCCUS PYOGENES. (*Stengel.*)

**M. cereus albus.**—Found in pus, singly or grouped, not motile, 1.15 $\mu$ diameter. Small white colonies on plates, superficial waxy streak in gelatine and agar tubes with edges elevated, also on serum and potato; grows at 30-37° C. and does not liquefy gelatine. Causes suppuration, usually associated with other forms.

*Stains,* with usual methods.

[1] In the descriptions of bacteria, plus and minus signs are used to denote behavior with Gram's method, G + meaning that an organism stains with it, G. — that it is decolorized.

**M. cereus flavus** differs from last by producing yellow pigment.

**Streptococcus pyogenes.**—Found in pus and erysipelas, not motile, in linear series of 20-40 cocci, 0.4-1.0 $\mu$ diameter, aërobic.

*Culture.*—Gelatine. On plate, colonies small, round, granular, brownish, edges raised; middle sunk; non-liquefying. Superficial growth in tubes. Agar about the same. Grows slowly at 37° C. and is apt to die out.

*Pathology.*—Alone or with other cocci it is found in suppurations, erysipelas, malignant endocarditis, otitis; often associated with diphtheria and tuberculosis.

*Stain,* usual dyes; G. +.

**M. tetragenus.**—Found as saprophyte in lung diseases of man, not motile, in pairs and fours, facultative aërobic. Grows as small white granular colonies on plates; on agar, serum and potato, heavy white film. Kills mice and guinea-pigs, not rabbits or field mice.

*Stains,* with usual dyes; G. +.

**Diplococcus of Pneumonia.**—Found in sputa of lobar pneumonia, exudate of meningitis, at times in saliva of healthy persons, non-motile, aërobic, 2-6 in series with common capsule which is lost in culture media.

*Culture.*—Gelatine. Small white, sharp-edged colonies, not liquefying; on agar almost invisible; on serum, transparent moist film. T. 24-42°, best 37° C.

*Pathology.*—Probably the cause of croupous pneumonia, but has been found in joint lesions, serous inflammation and meningitis.

*Stain,* usual dyes; G. +.

**Diplococcus intracellularis of Meningitis.**—Found in exudate of epidemic meningitis, not motile, in pairs, fours and short chains, aërobic.

*Culture.*—Does not grow on gelatine or potato, scanty in beef broth and on agar, best on blood serum mixture forming very

small colonies, smooth and round but may coalesce; requires frequent transplanting. T. 36° C.

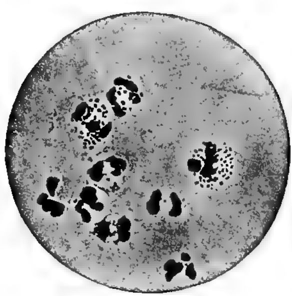
*Pathology.*—Causes epidemic cerebro-spinal meningitis; pathogenic for dogs and small rodents.

*Stains,* usual; G. —.

**Diplococcus of Gonorrhea.**—Found in cells of gonorrheal inflammation, both in protoplasm and nucleus of pus cells, in lesions of urethral mucous membrane, joints, etc., in this disease; not motile, aërobic, arranged usually in twos with slightly concave surfaces opposed, 0.8-1.5 $\mu$ diameter; when its virulence is attenuated it is found outside of the cells and is called pseudo-gonococcus.

*Culture.*—Not on gelatine. On human blood serum, smooth, thin, gray or yellow film, edges become more clearly distinguishable later, very slow; on albuminous urine and acid gelatine also; surrounding the colony there may be irregular ill-defined extension. T. 37° C. (25-38° C.).

FIG. 59.



GONOCOCCI. (PHOTO.)
For the most part enclosed in pus cells.

*Pathology.*—Causes catarrhal, suppurative inflammation of mucous membranes; has been found in joints and in heart (malignant endocarditis), pyo-salpinx, peritonitis, conjunctivitis.

*Stain,* usual; G. —.

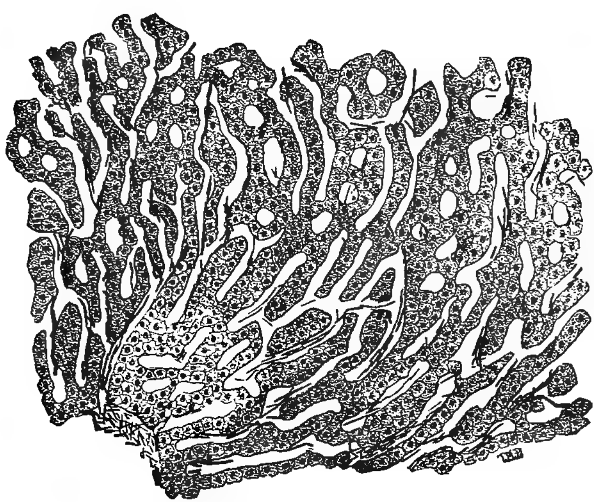
**Diplococcus of Trachoma.**—Found in lesions of trachoma, usually in pairs, like gonococcus but smaller and less distinct, not motile, aërobic. Grows as a shiny film on most media with little beads along the stick; not liquefying. T. 35° C.

Other cocci have been found in certain skin diseases, as pemphigus, pityriasis rosea, etc., and many forms among lower animals both resembling and differing from those in man.

## Pathogenic Bacilli.

**Anthrax.**—Found in blood of animals infected, not motile, aërobic and facultative anerobic; rods with square ends, 1-1.25 $\mu$ broad by 3-20 $\mu$ long, single, grouped and in filaments.

FIG. 60.



BAC. ANTHRACIS IN LIVER. (*Delafield and Prudden.*)

*Culture.*—Grows on all media, as a film on potato, in tree form in gelatine stab; liquefies both gelatine and serum. T. 12-45° C., best 37° C.: spores formed toward the higher limit in

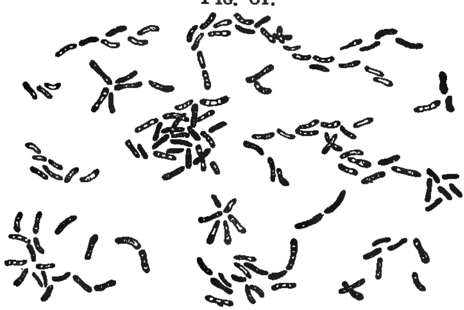
cultures, never in the blood. Colony peculiarly marked by wavy lines which start from edge and return, like locks of hair displayed. Very resistant especially the spores.

*Pathology.*—Cause of anthrax carbuncle, malignant pustule and wool-sorter's disease in man; charbon, splenic fever in herbivora.

*Stain,* usual; G. +.

**Anthrax, Symptomatic.**—Found in body fluids of infected animals, motile, flagellate, anerobe, delicate rods singly and paired, 0.5 μ broad by 3-5 μ long, ends round.

FIG. 61.



BAC. DIPHTHERIAE. (*Stengel.*)

*Culture.*—All media. Liquefies gelatine, appears as irregular granular colonies with thick center and radiate branches, in stab forms gas. T. 13-70° C., best 37° C.

*Pathology.*—Cause of symptomatic anthrax, man and animals.

*Stain,* usual; G. imperfectly.

**B. coli communis.**—See typhoid.

**B. diphtheriæ.**—Found in the membrane, not motile, aërobic, facultative anerobic, rods straight or a little curved, 0.3-0.8 μ broad by 2-4.5 μ long, stain markedly at the ends.

*Culture.*—Usual media; on potato hardly visible for a time, then a thin dry film with resistant feel; in gelatine stab small

colonies form along the stick and join to make a gray line; best medium blood serum; milk, agar and alkaline broth also. On serum in 6-24 hours a thin white layer forms, sometimes a little yellowish, with minute colonies near the edge. T. 20-40°, best 37° C.

*Pathology.*—Causes inflammation of varying severity on mucous surfaces and wounds with production of false membrane, made of fibrin chiefly, with bac. diphtheriæ in its meshes; associated with strepto- and staphylococci usually, so that the effect on the organism is of a mixed infection. After recovery the bacillus persists in mouth and nose for weeks; attenuated forms called pseudo-diphtheria bacilli.

*Stain,* usual, especially Löffler's methylene-blue; G. +.

*Diphtheria antitoxin* is prepared in flat-bottomed sterile glass flasks; at first it was thought necessary to keep a current of moist air running through the flask but this is proven to be superfluous. Beef broth with 2 per cent. peptone is put in the flask and sterilized, inoculated with vigorous bacilli and put in the incubator at 37° C.; in three or four weeks enough toxin has formed. The broth is then filtered under strict precautions through a porcelain filter (Pasteur-Chamberlain), and kept in the dark in sterile, well-stoppered bottles. Guinea-pigs (average 300 gm.) die in 48-60 hours from the injections of 0.1 cc. of the filtrate.

To immunize, dilute the filtrate with 25 per cent. Gram's fluid, inject a rabbit with 0.5 cc. of the mixture; after the reaction has quite disappeared (slight fever, increased pulse), inject a similar amount with less iodine solution. A point is reached where the iodine is left out and the animal can take as much as 100 times the amount fatal to a non-immunized rabbit. Of all animals the horse has been found most satisfactory for practical use as it bears large doses, thus shortening the time, and furnishes large amounts of serum. The antitoxic serum is obtained by drawing blood from a vein by a cannula into sterile vessels under strict antisepsis. To preserve the serum camphor,

tricresol, carbolic acid and other chemical antiseptics may be added, but with careful methods the serum is sterile and does not require such additions, which are undesirable.

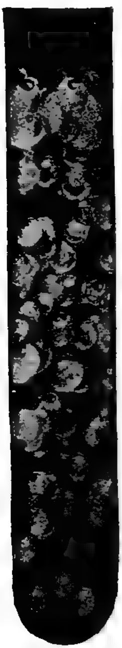
The value of the antitoxic power of serum thus obtained is based upon the least dose of toxin which is fatal to a given weight of animal. Several guinea-pigs may be selected, as nearly of a size as convenient (about 250 gm.) and each receives an injection of toxin, the dose varying for each; by the fourth or fifth day some will have died, and the minimum dose of toxin is taken as that which will kill 250 gm. of guinea-pig in 4-5 days. This should be subjected to further trial on other animals till determined beyond doubt.

The serum remains to be tested, and a unit of measurement established. This is done when it is learned how much serum will protect against the minimum fatal dose of toxin, *only it is stated as ten times the amount of antitoxin* which is effective *against ten times the minimum fatal dose of toxin.* Thus several doses of toxin are known to contain ten times the minimum fatal quantity, and varying amounts of antitoxic serum are added to these; to the first 0.01 cc., to the second 0.05 cc., to the third 0.1, to the fourth 1.0, and to another a higher amount. These mixtures of toxin and antitoxin, in which the latter element alone varies, are injected into guinea-pigs. That mixture is held to be effective which, with the lowest proportion of antitoxic serum, has prevented fever and local swelling; it is considered as one tenth of a unit. If this may have been the second of the preparations ten times the proportion of serum gives the antitoxin unit, in this case 0.5; in other words that amount of serum contains one immunity unit of antitoxin serum. Three strengths usually occur in the shops, a weaker for preventive inoculation, a stronger for treatment (by hypodermic injection) when the case is seen early in the disease, and a stronger yet for cases seen after the first 24 hours; more than one injection may be required. When the serum acts favorably the local and the general symptoms soon begin to improve.

It is but fair to add that the value of serum therapy is still contested by many careful writers, who contend that deaths from lung and kidney complications are more common under it and practically keep the mortality where it was before antitoxin treatment; and also that a large part of the apparent improvement since the introduction of antitoxin is to be explained by improved general hygiene and affects other diseases, not treated in this manner, to even a more marked degree than diphtheria.

**B. influenzæ.**—Found in mucus and discharges from nose and bronchi of infected persons, less often in blood, not motile, aërobic, in twos or short chains, 0.4 $\mu$ by 0.8-1.2 $\mu$, sensitive.

FIG. 62.



BAC. EDEMATIS MALIGNI. (*Stengel.*)

*Culture.*—Grows with difficulty on agar streaked with fresh sterile blood, as very fine drops like dew. T. 28-60°, best 37° C.

*Pathology.*—Cause of influenza in man and monkeys. A similar organism has been isolated from the lung of post-diphtheritic pneumonia.

**B. edematis maligni.**—Found in garden earth, intestines of normal animals and connective tissue of infected animals, perishes in blood; motile, anerobic, rods 3-5.3 $\mu$ long, by 1 $\mu$ broad, ends rounded, may form long series.

*Culture.*—Grows on usual media, liquefies gelatine, on agar plate grows in the deep layers as white opaque spots; in gelatine stab forms white cloudy colonies and gas, especially if glucose is present. T. best 37° C.

*Pathology.*—Cause of malignant edema, cattle nearly immune, cat and dog less so, small rodents very susceptible. Not found in the blood till long after death because of oxygen in it.

*Stain,* usual; G. —.

**B. pneumoniæ.**—Found in sputa and lung of croupous pneumonia, not motile, aërobic, rods short enough to resemble cocci

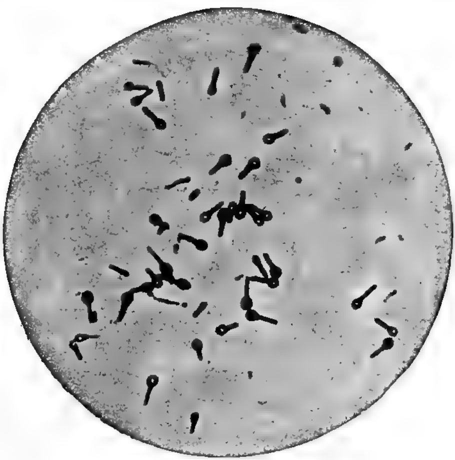
or longer, often in short chains with a common hyaline capsule, measurements uncertain.

*Culture.*—All usual media. In gelatine stab makes a characteristic nail-shaped figure; forms gas, does not liquefy gelatine. T. 14-40° C., best 37° C. Spores?

*Pathology.*—May cause croupous inflammation in man, dog, guinea-pig.

*Stain,* usual; G. —.

FIG. 63.



BAC. TETANI. (*Stengel.*)

**B. pyocyaneus.**—Found in green pus, motile, aërobe, rods 0.5 $\mu$ by 1.5 $\mu$, grows on gelatine, potato, agar, milk; liquefies gelatine; on solid media makes transparent film in 24 hours, which turns greenish and medium fluorescent. T. best 26-37° C.

*Pathology.*— Causes a green color in pus, may produce septicemia as it is virulent in pure culture.

*Stain,* usual; G. +.

**B. pyogenes fetidus.**—Found in foul pus, motile, aërobe, short rods with rounded ends, singly and chains, 0.5 $\mu$ by 1.4 $\mu$.

Grows in broth and on solid media as light gray film turning brown as it becomes thicker, shiny, rapid grower, odor disgusting, does not liquefy gelatine. T. 30-37° C. Fatal to small rodents.

*Stain,* usual; G. +.

**B. pestis.**—Found in lymph nodes, spleen, blood and feces of patients dying of bubonic plague, flagellate, motile, aërobe and facultative anërobe, 1.7 $\mu$ by 2.3 $\mu$, swollen and staining on ends, gives appearance of diplococcus.

FIG. 64.

BAC. TYPHI WITH FLAGELLA. (*Stengel.*)

*Culture.*—Various media, glycerine agar makes white or blue-white colonies; in gelatine stab makes tree form, does not liquefy it; best medium alkaline peptone with two per cent. gelatine; forms acid and indol; in presence of salt (3 per cent. NaCl) at 37° C. forms yeast-like involutions.

*Pathology.*—Cause of bubonic plague in man, fatal to small animals, spread by rats and flies.

*Stain,* usual; G —.

**B. typhi abdominalis.**—Found in water and milk from contact with infected person; urine, feces of the sick; spleen, intestine and gall-bladder of the dead; motile, flagellate, aërobic, facultative anerobic, single or grouped, straight rods with round ends, 0.5-0.8 $\mu$ by 1.0-3.0 $\mu$ long.

*Culture.*—Potato, agar, gelatine, serum, milk, not liquefying. On potato characteristic invisible film, moist and shiny, resistant to touch. T. 15-45° C., best 37° C.; spores form at 30-42°, one in each rod, at the end.

*Pathology.*—Cause of typhoid fever in man; after alkalizing the stomach and arresting peristalsis in animals, feeding with typhoid cultures causes intestinal lesions; injected into the blood causes septicemia.

*Stain*, usual; G. —.

Chief differences between b. typhosus and b. coli communis:

| | B. TYPHOSUS. | B. COLI COMM. |
|---|---|---|
| Colonies on gelatine plates. | On surface large, gray-white, edges irregular, turn yellow brown; in the depth, dark with regular edges; non-liquefying. | Colonies dirty white, turn dirty yellow, round or oval, margins smooth; non-liquefying. |
| Potatoes. | Faint gray white film on potato usual. | Growth slimy and yellow, or brown. |
| Milk. | Acidulated, not coagulated. | Acid reaction, coagulated in one to three days. |
| Broth. | Becomes turbid, no indol. | Turbid, indol in 24-48 hrs. |
| Ferment. | None. | Always with sugars, producing gas. |
| Neutral red. | Color persists. | Turns yellow. |
| Potassium nitrate. | Not reduced. | Reduced to nitrite and then ammonia. |
| Litmus-lactose-agar plate. | Blue colonies, no reddening. | Pink colonies, medium red. |
| Suppuration. | Sometimes in post-typhoid abscesses, as of parotid. | More strictly pyogenic. |
| Widal reaction. | Positive with blood from typhoid patient or animal immunized. | Negative. |

**B. mallei.**—Found in farcy buds, mucous discharges and exudates of infected man or animal (especially horse and ass), slight motility, aërobe, facultative anerobic, rods like tubercle bacilli but shorter and thicker, 0.4 $\mu$ by 2-3 $\mu$ with irregular staining simulating spores.

*Culture.*— Potato, makes yellow slimy film. honey-like, turning reddish brown; on gelatine round dots with undulating margin; on agar scattered honey-like drops. T. 25-42° C., best 37° C.

*Pathology.*— Causes glanders and farcy in animals, transmissible to man and rodents.

*Stain,* usual, especially alkaline solutions, needs a long time with quick decolorization; G. —.

**B. tetani.**—Found in earth which has been manured and in discharges of wounds after infection; motile except with spores, anerobic; in straight rods, racket and spindle shapes and chains, 0.5-0.8 $\mu$ by 1.2-3.6 $\mu$, many involution forms.

*Culture.*— Best, alkaline gelatine with 2-per-cent. dextrose, also on agar, serum, and in broth; liquefies gelatine, forms gas; in depth of gelatine stab single colonies form at right angles to stick; end spores common and resistant. T. 14-42° C., best 36-38° C.

*Pathology.*— Cause of tetanus in man, fatal to mouse, rabbit, guinea-pig.

*Stain.* usual; G. +.

**Rhinoscleroma Bacillus.**—Found in nose and throat of infected individuals, in the tissue, not motile, facultative anerobe, short rods with ends rounded, some like oval cocci, single, paired and chains, 0.5 $\mu$ by 1.5 $\mu$.

*Culture.*—Forms white layer on usual solid media, nonliquefying; in stab makes nail figure but the head is transparent. T. best 36-38° C. Retains its capsule in culture media.

*Pathology.*— Cause of rhinoscleroma; no effect on animals.

*Stain.* usual; G. +.

**B. aerogenes capsulatus.**—Found in fluid of tissue destruction in emphysematous necrosis and gangrene, not motile, anerobic, rods like anthrax, ends square or rounded, 1.0-1.25 $\mu$ by 3.0-6.0 $\mu$, pairs, clumps and short chains, capsuled in agar at times, no spores.

*Culture.*— Deep in agar and gelatine stabs as small lenticular disks with knobs or feathery projections, white or gray, forms gas, liquefies gelatine slowly; T. 36-40° C.

FIG. 65.

PETRI AGAR PLATE. (*Delafield and Prudden.*)

Made by spreading scrapings from the mouth over sterilized nutrient agar; after 48 hours in the thermostat the light "colonies" develop.

*Pathology.*— Causes emphysematous gangrene, found in the cadaver early in decomposition; may explain "air embolism" of the lung after parturition.

*Stain.* usual; G. +.

## Pathogenic Spirilla.

**Cholera asiatica.**—Found in "ricewater" feces and intestinal contents of infected persons, motile, with end flagellum, aërobe and facultative anerobe, in short arcs and spirals, "comma" forms, or longer winding filaments, 0.5 $\mu$ by 0.8-1.5 $\mu$, no spores.

FIG. 66.

SP. CHOLERAE ASIATICAE. (*Stengel.*)

*Culture.*—Usual culture media, liquefies serum and gelatine; on plate forms white or yellow-white colonies with granular surface and irregular margin; in gelatine stab liquefaction begins at surface and proceeds downward, making inverted cone with air bubble at top; in broth and liquid media forms indol and nitrates, giving "cholera red" reaction with pure HCl or $H_2SO_4$; milk not coagulated. T. 14-42° C., best 37° C.

*Pathology.*— Cause of Asiatic cholera in man; similar lesions in animals after neutralizing the gastric juice and arresting peristalsis.

*Stain,* usual; G —.

Spirilla resembling that of cholera asiatica:

Finkler-Prior; obtained from feces of cholera morbus, like former in shape, growth and indol formation, but longer, more slender (0.5-0.6 $\mu$ by 0.6-2.5 $\mu$) and coagulates milk; in gelatine stab grows faster and liquefies faster; motile, with end flagellum.

Deneke's tyrogenicum. Found in old cheese; liquefies gelatine faster than s. choleræ but not so fast as Finkler's; motile, end flagellum.

Spirillum of Metschnikoff, found in feces of fowl cholera, shorter and thicker than cholera asiatica, but cultures very similar; not pathogenic for man; kills chickens, pigeons and guinea-pigs.

Spirillum sputigenum, isolated from saliva, resembles cholera, but longer and thinner; not cultivated in any medium so far.

**Spirillum of febris recurrens.**—Found in blood of patients with relapsing fever during the paroxysm, vanishes afterward; very motile, undulating pliant filaments with pointed ends, 0.1 $\mu$ by 20-35 $\mu$ or longer, spirally twisted, no spores.

*Culture.*— Not yet propagated outside the body.

*Pathology.*— Constant in relapsing fever; transmissible to monkeys by injecting blood of patient.

*Stain,* usual; G —.

## Organisms of Infectious Granulomata.

**Bacillus of Leprosy.**—Found in skin and other lesions of leprosy, not motile, rods like tubercle bacilli, but ends sharper and take basic stains better, 0.5 $\mu$ by 4.0-6.0 $\mu$; spores?

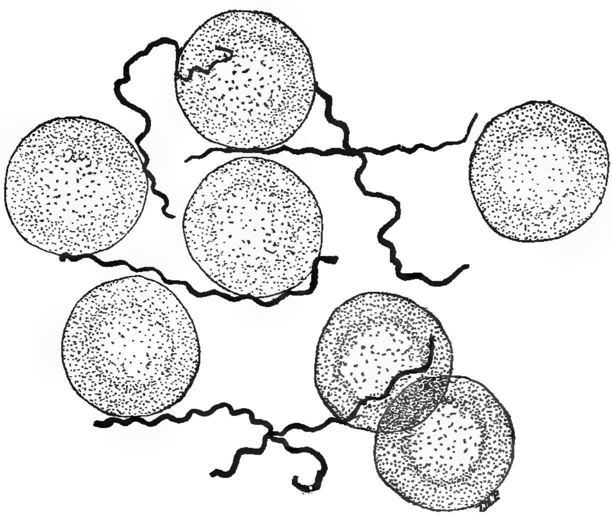
*Culture.*— Not yet successfully grown on artificial media.

*Pathology.*— Constant in leprosy of all forms.

*Stain,* usual, but with difficulty; G. +.

**Bacillus of Syphilis.**—Described as found in most lesions and exudates of syphilis, resembles tubercle bacillus, but, like the lepra organism, cannot be cultivated or transmitted to animals; causal relation to syphilis questionable. A similar bacillus found in secretions from Tyson's glands (smegma).

FIG. 67.



SPIROCHETE OF RELAPSING FEVER. (*Delafield and Prudden.*)

**Bacillus tuberculosis.**—Found in sputa and lesions of tuberculosis, non-motile, aërobic, rods straight or curved, ends rounded, 0.25 $\mu$ by 1.5-3.5 $\mu$, sometimes present oval unstained areas which suggest spore formation, branching forms have been found, closely resembles a rod bacillus from cow dung, as also the timothy hay bacillus.

FIG. 68.

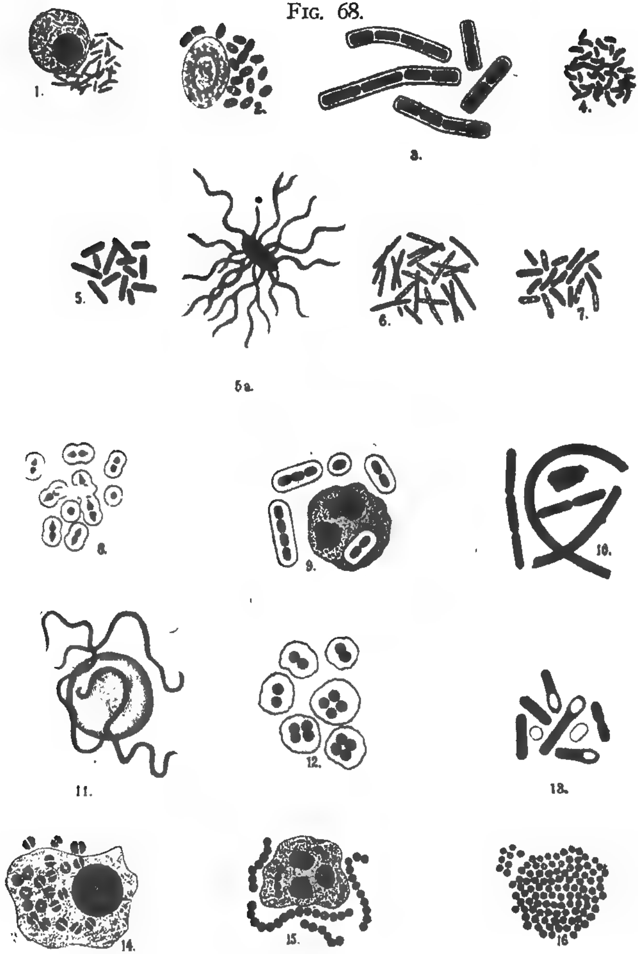
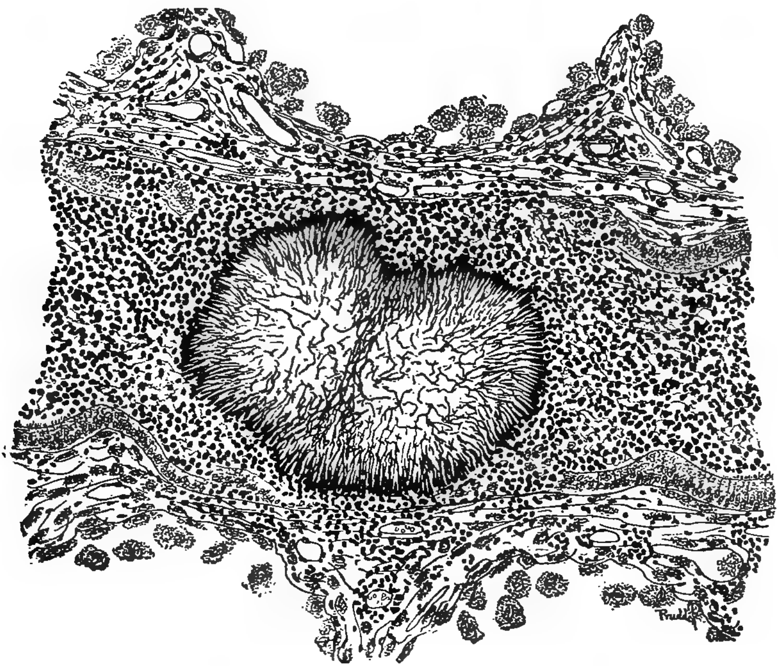



PLATE OF BACTERIA ON THE SCALE OF 1 TO 1,600. (*Birch-Hirschfeld.*)

1, bacilli of swine erysipelas; 2, bacilli of hen cholera about a red cell, from fowl's blood; 3, anthrax bacilli with capsule; 4, cholera vibrio; 5, bacillus typhosus; 5a, the same with flagella; 6, tubercle bacilli; 7, glanders bacillus; 8, pneumococcus of Fränkel; 9, bacillus pneumoniæ of Friedländer; 10, bacillus of malignant edema; 11, spirochete of relapsing fever; 12, micrococcus tetragenus; 13, tetanus bacilli with end spores; 14, gonococci; 15, streptococci; 16, staphylococci. The relative size of the organisms appears from the accompanying cells.

*Culture.*— On potato, serum, glycerine agar, in glycerine broth and milk; growth slow; on glycerine agar small white dots which join later to form "bread crumb" layer, wrinkled yellow-white film; more yellow on potato. T. 30-42° C., best 37.5°.

FIG. 69.



ACTINOMYCES. (*Delafield and Prudden.*)

*Pathology.*— Cause of tuberculosis in man, all forms; may be transmitted to many lower animals. Whether the bacilli from tuberculosis in animals are pathogenic for man is still disputed.

*Stain*, usual and special methods, Ziehl-Neelsen quick and satisfactory; G. +.

**Actinomyces; Ray Fungus.**—Found in lesions of the disease in man and animals, not motile, both aërobe and anerobe, in three forms:

1. Coccus, 0.5 $\mu$ diameter, perhaps the spores of
2. Long threads, slender or thick, often curved, may be slightly thicker on ends, not clubbed; anerobe.
3. Filaments distinctly club-shaped, radiating from a center which in tissues is often calcified.

*Culture.*—Anerobic, form alone pathogenic. On serum forms a thin gray, moist layer, made of fine transparent lines, parallel or woven; in 24 hours air hyphæ project and give the appearance as if sprinkled with chalk; as culture dries the white spots turn reddish-yellow or rusty, T. 33-37° C., with exclusion of oxygen.

*Pathology.*— Cause of actinomycosis in animals, less often in man.

*Stain,* yellow with iodin and picric acid, red with picro-carmin, blue with anilin gentian, cocci red with eosin; G. +.

## Appendix to Chapter IX.—Immunity.

Certain people, though exposed to infection by various disease-producing bacteria, appear but little liable to the attack, others who have had a disease may never have it again even when exposed. Such resistance to disease is called immunity. It may be natural, as where certain races of men or animals are less apt to take disease than others (the negro in some yellow-fever epidemics); or acquired, when susceptibility gives place to resistance. This acquired immunity may be either active or passive.

Active immunity follows an attack of a certain disease and secures immunity for that alone, which may last but a short time (erysipelas, cholera), or for a longer period (typhoid), or even for life (variola); or it follows inoculation of a virus weaker than necessary to cause the typical disease (vaccination against small-pox); or it follows inoculation by bacterial products apart from the organisms themselves. Passive immunity

is the term applied to the effect of a serum derived from an immunized animal and injected into one not immune, the theory being that in the blood of the former there is a chemical substance (antitoxin) which neutralizes the toxin in the donating animal, or otherwise it would show symptoms, and by borrowing its serum for the infected animal the toxin is opposed by the alien antitoxin. A local immunity is spoken of, but the term is of doubtful value.

THEORIES OF THE MODUS OF IMMUNITY.

1. The bacterial products accumulate in the infected organism to a percentage which inhibits further activity or growth (Chauveau).
2. The cells which have combated the agent of infection with success acquire and retain increasing power of resistance (Grawitz).
3. The germs having special localities of attack, the cells there develop resisting powers for the particular germ in question (Buchner).
4. The ameboid cells have the power of ensphering bacteria and digesting them; part of the ingested organism is returned to the serum in harmless form and excreted; the white cell breaks up (phagolysis) and sets free in the stream its resisting chemical element. The cells (phagocytes) thus "eating" bacteria are:
    1. Micro-phagocytes; eosiniphile and amphophile.
    2. Macro-phagocytes; large lymphocytes.
    3. Endothelial cells, of capillaries.
    4. Fibroblasts.
    5. Pseudo-plasma cells. (Metschnikoff; Phagocytosis.)

In many infections no phagocytosis has been observed. In others the phagocytosis follows the bacterial invasion instead of preceding it or occurring with it. In still others the bacterial activity is marked even where leucocytes are copious, as in the nodes. Sometimes

the bacteria survive the cells which englobe them; this is the case in gonorrhea. In many cases the bacteria actively invade the phagocyte instead of being passively taken up by them. Lastly, as a matter of fact, the phagocytes may take bacteria to places which they would not otherwise reach and there set them free to attack tissue: as when a non-motile tubercle bacillus is carried from the bronchial mucous membrane to a lymph node, or from the surface of a Peyer's placque into the lymphoid tissue. These are strong objections to the universality of the theory.

5. The fresh blood serum contains chemical bodies (alexins) which destroy bacteria; now extended to include various tissue fluids. These defensive substances, supposed to be proteids, are called sozins if naturally present in the serum, phylaxins if the result of immunization; the former destroy both blood cells and bacteria and are themselves destroyed by exposure to 55° C.; if they oppose the bacterium they are called myco-sozins, and if they counteract the toxin, toxo-sozins. The phylaxins, the true antitoxin, destroy neither blood cells nor bacteria and retain their properties after exposure to 80° C.; they also are divided according to their activity into myco- and toxo-phylaxins (Buchner-Hankin).
6. By far the most fruitful of the theories of immunity is the Side-Chain theory advanced by Ehrlich. It is difficult to grasp until one is familiar with the new words used to carry the new ideas.

On the analogy of the benzole ring, which preserves its nucleus of $C_6$ despite numberless changes in the side-chains, it is assumed that each living cell has a vital nucleus with which its identity is bound up. To this vital nucleus are attached side-chains, not absolutely necessary for the life of the cell, which act as

unsatisfied bonds and fix nutriment to the cell. These are thought to be of three varieties, countless in number, and have received the name *haptines,* or *receptors.* They are of three orders:

> I. Order.—The simplest, fix molecules of nutritive value, toxins and cellular products. Cast loose from the cell they may circulate in the blood and act as *antitoxin.*
>
> II. Order.—These receptors fix a more complex molecule with one of their affinities, and with another prepare it for the use of the cell by a quasi-digestion, acting like ferments.
>
> III. Order.—By one bond these receptors cling to the cell, by a second to the molecule attacked, and by a third they disintegrate the molecule. Separated from the cell they circulate in the blood as *amboceptors* or the *immune body.*

The Side-Chain theory of immunity assumes in the blood of an infected animal two kinds of elements which are engaged in poisoning the cells; both of these are essential or the poison can not unite with the cells. One of these combines with the cell and is called *haptophore;* the other, the *toxophore,* is then able to attack the cell. The haptophore unites with one of the cell's receptors, and the mechanism is thus seen to be a modification of that provided for the nutrition of the cell.

Since the union of a cellular element, or receptor, with the haptophore element of the introduced toxin, does not form a nutritive unit which the cell can use, it must either have or make other receptors, to unite with useful chemical compounds, or it must perish; and, thus stimulated to the manufacture of receptors, it may produce them in abundance, and they may separate from the cell, and circulate in the blood. There they come in contact with poison, of bacterial origin, for example, and neutralize it.

It has been proved by experiment that when an animal, as a rabbit (A), is injected with the serum of another animal, as the dog (B), every few days for five or six doses, the serum of A will precipitate the serum of B in a glass, though both are much diluted. When the red cells of B's blood are used for injecting, then A's serum will dissolve the red cells of B in the same conditions. The blood in the first case is said to contain an element called *precipitin,* and in the second, one called *hemolysin.* In a similar way a series of experimental products can be obtained, each specific in its action, to which the general name of *anti-bodies* has been given. Among these we have some which will neutralize ferments, called *anti-enzymes,* those which dissolve bacteria, called *bacteriolysins,* those which agglutinate blood cells, called *agglutinins,* etc.

The different destructions accomplished in this way are named according to .he cell involved. Consequently the words erythrolysis, myolysis, neurolysis, spermatolysis, and others of this kind, imply that red cells, muscle cells, nerve cells or semen had been used to inject an animal in order to obtain a serum specific in its power of destroying the special kind of cells employed.

When disease attacks a subject, and poison of bacterial origin circulates in its blood (it may be free or still in the bodies of the bacteria), the cells of the organism furnish something called the amboceptor, or immune body, which unites with the toxin and destroys it. If the supply of this immune body is plenty and potent, the patient resists the attack. The immune body of another person or an animal may be injected into his circulation to assist in the process. This is the basis of serum therapy. If he has already withstood an attack of the disease, his blood may have so many free receptors, or so much immune body, that he is refractory, or immune. This is what is meant by active acquired immunity.

The immune body and the complement act differently under various influences. For example, the complement is destroyed

by a temperature of 55° C., and is hence termed labile; the immune body resists 75°.

Various synonyms are used for the same thing, thus immune body, amboceptor, desmon, sensitizing substance, and intermediate body, all mean the same thing. The destructive principles are called *lysins* or *cytotoxins*. The special one acting in a given case is called variously complement, lysin, sometimes with another word like bacterio-lysin, alexin and addiment. In general, the amboceptor mediates between the destructive agency and the cell affinity sensitive to the former.

Bacterial poison are assumed to be of three grades of strength, toxin, weaker toxoid, and toxone; they all have haptophore elements.

# CHAPTER X.

## INFECTIOUS DISEASES.

WHEN microörganisms enter the body, proliferate and cause disease, the act is called infection and the disease infectious. Bacteria may cause local effects, stopping small vessels or setting up productive or degenerative cell and tissue changes; they gain entrance usually through some solution of the body coverings, cutaneous or epithelial. Their constitutional effects may be due to the absorption and distribution of their products alone (intoxication, as tetanus), or the bacteria may invade every tissue or selected parts (true infection, as anthrax). The terms toxemia for the former and septicemia for the latter are often used for these conditions. Infection may be congenital; tuberculosis, syphilis and anthrax sometimes pass from mother to child via the placenta. Terminal infection is the unusually rapid and hence fatal invasion of a patient already weakened by some disease. Mixed infection is seen where two organisms coexist in the tissues, as diphtheria and streptococcus, tubercle bacilli and pus organisms. Many of the infectious diseases are communicable directly from man to man (scarlet fever), others through an intermediate organism (malaria, yellow fever), others apparently not at all (tetanus). When bacterial products occur in the blood, the condition is called sapremia; if pus organisms occur in the blood without producing secondary pus foci, septicemia; if present and causing multiple abscesses, pyemia.

### Pathogenic Bacteria as the Cause of Disease.

**The Pus Group.**—Beside the usual pus organisms, strepto- and staphylococci, many other bacteria are positively tactic to

pus corpuscles and wherever they lodge set up suppuration, locally as boils, pustules and abscess and generally as suppurations of joint surfaces and serous membranes. They often play a part as the second element in mixed infections, as in tuberculosis of the lung, where there is no cavity formation and little fever or emaciation until the action of pus organisms is marked in tissues already weakened by tubercle bacilli. Pus confined in the tissues gives rise to intoxication through absorption of toxin and that from streptococci is specially virulent. Other pus organisms are b. coli communis, b. pyocyaneus, b. proteus, diplobac. pneumoniæ, etc. A special form of disease due to a coccus is erysipelas, the organism of which appears to be identical with streptococcus pyogenes.

**Post-mortem Changes after Septicemia and Pyemia.**—There may be no gross lesion; the chief finding may be remarkably rapid decay of all the tissues, hemorrhages passim, general congestion of all organs, softening of the spleen and post-mortem staining by blood coloring matter; abscesses may occur in many organs and in the joints, with pus on serous membranes; there may be venous thrombi at the seat of the primary pus focus and multiple emboli of infected material.

**Epidemic Cerebro-spinal Meningitis.**—An acute suppurative inflammation of the meninges of brain and cord, especially the pia; serum, fibrin and pus present in varying amounts, over the whole cortex and throughout the cord, or localized, or so scanty that the microscope is required to detect the exudate. Fluid obtained during life by puncture of the lumbar spine may contain cells with the diplococcus intracellularis inside; the usual pus forms and pneumonia diplococci have also been found. Other lesions are hemorrhages in skin and serous membranes, abscesses in joints, degenerations in voluntary muscles and cloudy swelling of parenchymatous organs.

**Croupous Pneumonia.**—The diplococcus pneumoniæ is often a cause of lobar pneumonia, but not the only one. It may occur in the healthy mouth and lung and has been the ap-

parent cause of pleuritis, otitis, meningitis, peritonitis and other suppurative diseases. For gross and microscopic appearances see p. 397.

**Gonorrhea.**—This disease is caused by the diplococcus known as gonococcus and is an acute, very contagious inflammation of exudative type affecting mucous and serous surfaces. Beside the changes in the urethra, this organism has caused inflammation of the conjunctiva, peritoneum, joints, endocardium and fallopian tubes.

**Anthrax.**—Splenic fever or malignant pustule is rare in man in the United States. The germ gains entrance through skin abrasions and by inhalation and causes local or general effects. Post-mortem decomposition is rapid, blood not much coagulated, bleeding common on surfaces, edema or inflammation of lung, spleen swollen and soft; microscopically the bacilli are found in numbers in capillaries of liver, kidney and lung.

**Diphtheria.**—The false membrane may be found on mucous surfaces of the upper air passages or in the bronchi, and in the stomach if swallowed; it is formed of fibrin, pus, epithelia and red cells, with diphtheria bacilli and pus organisms, and under it the tissues may be necrotic; or there may be no membrane, the mucous surfaces being simply congested and inflamed. Where the false membrane has sloughed off there may be ulceration, the lymph nodes are swollen or softened, parenchymatous organs present foci of necrosis, nephritis is usual, degeneration and inflammation of the nerves common. Part II, p. 445.

**Influenza.**—Post-mortem appearances are not typical, being those of the fatal complication, very commonly pneumonia.

**Bubonic Plague.**—The characteristic lesions are swollen and suppurating lymph nodes, especially of groin and axilla, but in some cases there are no buboes, only the lesions of fatal intercurrent disease, as lobar pneumonia; the punctate hemorrhages common to all diseases with fever and disorganization

of the blood are also present, with blood-stained serum in the body cavities.

**Tetanus.**—The central nervous tissues are apt to be intensely congested and the wound which was the port of entry may be found; microscopically intense active hyperemia of the cerebral capillaries with cellular exudate in the perivascular spaces and degeneration of ganglion cells. The bacilli occur only at the wound; sometimes when there is no evident wound it is assumed that they enter through the alimentary or other mucous membrane. In tetanus neonatorum the wound is the cut surface of the cord.

FIG. 70.

GLANDERS, GROSS LESION. (*Birch-Hirschfeld.*)

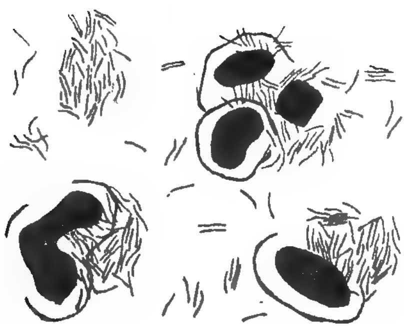
Acute infection by bacillus mallei. Ulceration developed in 8 days from pemphigus-like vesicles.

**Typhoid** having so distinct a lesion in the intestine will be treated in p. 475, Chap. XVI., but there are cryptic cases where the intestinal lesion fails (as with intra-uterine infection), and in any case the more distant lesions may be very marked, as splenic and hepatic necrosis, parotic abscess, degeneration of voluntary muscles, etc.

**Glanders.**—The lesions are chiefly located about the upper respiratory tract, elevated areas on the mucosa of the nose which

soften, ulcerate and join to form excessive loss of tissue, with yellow necrotic floor and purulent discharge; similar nodules in larynx and lung and at times in the alimentary canal; boils, carbuncles and abscesses occur in the skin and between the muscles, and nodules are found in spleen, liver, testes, etc.; osteo-myelitis and joint suppurations occur. When small these nodules resemble miliary tubercles. "Farcy buds" occur in the skin, especially when an abrasion is the point of entry. Microscopically there is an infiltration of small leucocytes, proliferation

FIG. 71.



LEPRA BACILLI IN THE LARYNX. (*Birch-Hirschfeld.*)

of epithelioid cells, hyperemia and rhexis, necrotic changes and softening, and, near mucous surfaces, increased production of altered mucus which excoriates the skin adjacent.

**Rhinoscleroma** presents nodular thickening of the tissues of the nose and adjacent parts, the lip, pharynx and larynx, associated with ulceration of the mucous parts involved. Microscopically the new tissue resembles granulation tissue, and between the cells are the bacilli, which occasion hyalin degen-

eration also; since the disease cannot be reproduced in animals the exact relation of the bacillus is undetermined.

**Cholera Asiatica.**—The chief lesions are those of the alimentary canal and will be treated in p. 474.

**Relapsing Fever.**—Beside the presence of the spirochete in the blood there are no characteristic lesions; the tissues may be jaundiced, parenchymatous organs may be softened and degenerated, especially the spleen, which may be large and soft enough to rupture before death or may contain infarcts, and abscesses from their softening; and other lesions associated with high temperature occur, submucous ecchymoses, etc. Changes in the long bones, both degenerative and productive.

**Variola.**—The post-mortem appearances are those of the dermatitis, macule (seldom persists), papule, vesicle, umbilicated vesicle, pustule, ulcer and scab; and those of fever and pus infection, various bleedings, degeneration of organs, and inflammation of mucous membranes; severe streptococcus infection is always present. A protozoan organism is described as the cause of the disease. This presents two forms, one of them invading the body of the cell and the other its nucleus. In the latter place it makes ring forms which segment. The former alone is present in vaccinia. These two forms are supposed to be the two sexes. In variola the organism has been found in the papule, the pustule and the blood.

**Rabies, typhus, pertussis, scarlet fever, measles and yellow fever** have no constant and characteristic post-mortem changes, and the lower organisms which undoubtedly cause them are still to be discovered. It is supposed that some of them are beyond the limit of visibility in the microscope, even with the highest magnification.

## The Infectious Granulomata.

**Lepra Arabum. Elephantiasis Grecorum, Leprosy.**—Infectious disease of chronic course, characterized by the formation of granulation tissue under the influence of the lepra

bacillus, in conditions of bad sanitation; the skin shows tumor-like nodes (l. tuberosa) or patches (l. maculosa), the nerves are apt to be involved (l. anesthetica). The face is often attacked early, hyperemic spots appear and fade again but for

FIG. 72.

NODULAR FORM OF LEPROSY. (*Birch-Hirschfeld.*)

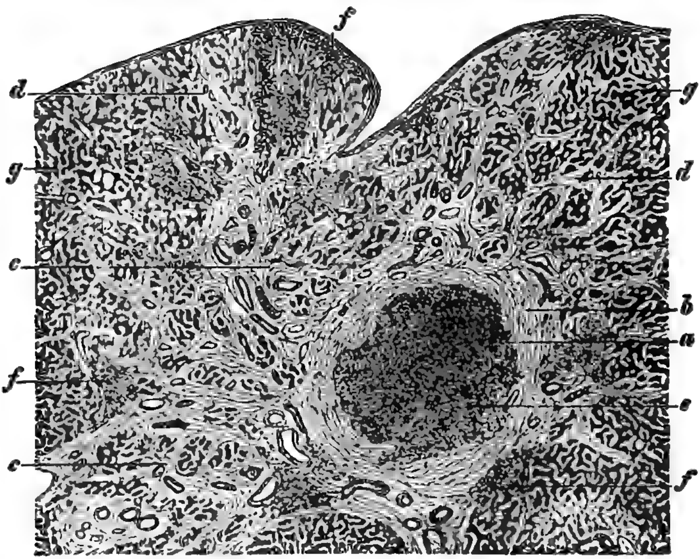
some pigment, or swell into nodules, arranged singly, in groups, or confluent; composed of small and large round cells, especially about the hair-follicles and reaching into the subcutaneous tissue, with stellar and spindle cells associated. The adjacent tissue atrophies, the nodules persist for a time, then soften and

form ulcers. Such nodules may occur on the back of the hand (palm exempt), the extensor aspect of joints, and in mouth, tongue, gum, larynx, etc. Adjacent lymph nodes are apt to be swollen, hard and yellow, from connective-tissue hyperplasia and fatty degeneration of the cells. Fever may accompany the formation of new nodules, nephritis is common, tubercle infection often occurs late in the disease, amyloid changes are found in ulcerating forms. The disease may last ten years or more before ending fatally. Liver, spleen and testis may present diffused or localized connective-tissue hyperplasia. The lepra bacilli are found in all affected tissues and in the endothelium of the vessels, free and in cells, giant and others. The disease is said to be hereditary and contagious, but slightly in each case, seldom appears till after the third year of life, most common in males from 20 to 30 years, and in the United States only among immigrants.

**Syphilis.**—The disease is peculiar to man and consists of a local initial lesion, the chancre, with constitutional symptoms after the lapse of some weeks usually, followed by secondary and even tertiary constitutional changes with long intervals between. The initial sore may be an eroded papule, or an ulcer on an indurated base, associated with moderate swelling of the corresponding lymph nodes, made up of small round-cell infiltration, connective tissue proliferation and hyaline change in the vessel walls and tissue about them, with more or less complete obliteration of their lumina; the proliferation and hyaline changes are the essential ones, inflammatory follow. The chancre may occur on any surface of the body within reach of the virus, but in the majority of cases it is found on the external genitals. The secondary lesions are varied, most commonly a skin eruption with fever, constitutional disturbance, and anemia from destruction of red cells and increase of white; condylomata, local elevations of the skin due to the irritation of secretions, often about the perineum, consisting of marked infiltration of the papillæ and epidermis with round cells, ac-

companied by edema, plasma cells abundant; these lesions occur as long as 6-8 weeks after the chancre. In some cases, usually after two years, tertiary changes occur, involving bones and viscera, consisting of tumor-like connective-tissue growths with a tendency to caseous and other degeneration — the syphilitic

FIG. 73.



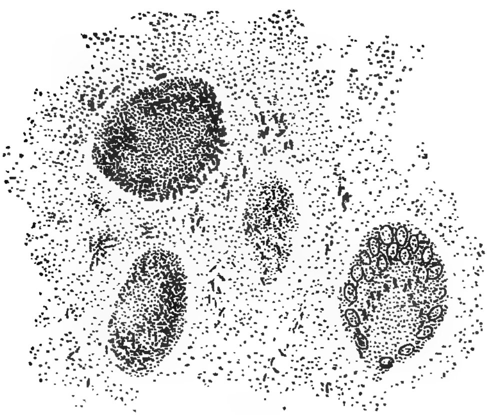

GUMMA OF THE LIVER. (*Ziegler.*)

*a*, Caseous nodule; *b*, connective tissue, at *c*, enclosing atrophic liver cells, at *d*, radiating into the liver parenchyma; *e*, cellular foci at edge of caseous nodule and in fibrous bands at *f*; *g*, liver tissue.

gumma. In the gross such gummata are hard and dense, made up of a band or series of bands of fibrous tissue enclosing dry, caseous masses, often several, with indications of a wide meshwork between; through softening and absorption only an irregular scar may be left. Microscopically the remains of cells and nuclei are found in a granular fatty mass; the vessels

of the part are narrowed or closed by proliferation of the intima, round and spindle cells may appear in the adventitia, the media is less often involved. Giant cells may be found. Such gummata in bones (skull, tibiæ), may soften and destroy them; they are common in liver, testis, spleen and brain. The fetus may be attacked before birth and die in utero, or if born alive falls a victim to diarrheal diseases. The upper incisors of the second dentition are notched on the free edge, other teeth may

FIG. 74.



TUBERCLE BACILLI IN GIANT CELLS. (*Birch-Hirschfeld.*)

From chronic peritoneal tuberculosis.

be imperfect, conical and peg-shaped. Gummata may occur in these children even when dying in the first week, and they may be soft, small and in beginning necrosis or already caseous. Other lesions are " white " pneumonia, induration of spleen and pancreas, hyperplasia and fatty degeneration of the long bones at the epiphyseal lines, and skin lesions.

**Tuberculosis.**—The name tubercle, applicable to any small nodule, is now reserved for the result produced by tubercle

bacilli in the various tissues; distinctions of color, white, gray or yellow tubercle, are not considered of importance at present. The smallest tubercles are called miliary, larger are conglomerate, but any tubercle visible to the naked eye is made up of smaller groups, each called a granuloma; tissue not presenting nodules but containing much tubercle tissue is said to be infiltrated. Histologically the tubercle is a collection of epithelioid cells with large oval nuclei and glistening nuclear bodies; between these cells there is a delicate fibrillar basement substance which is more apparent in older forms. In many tubercles there

FIG. 75.

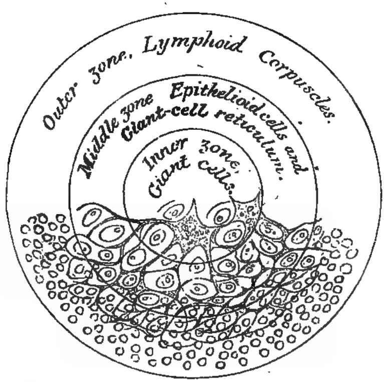
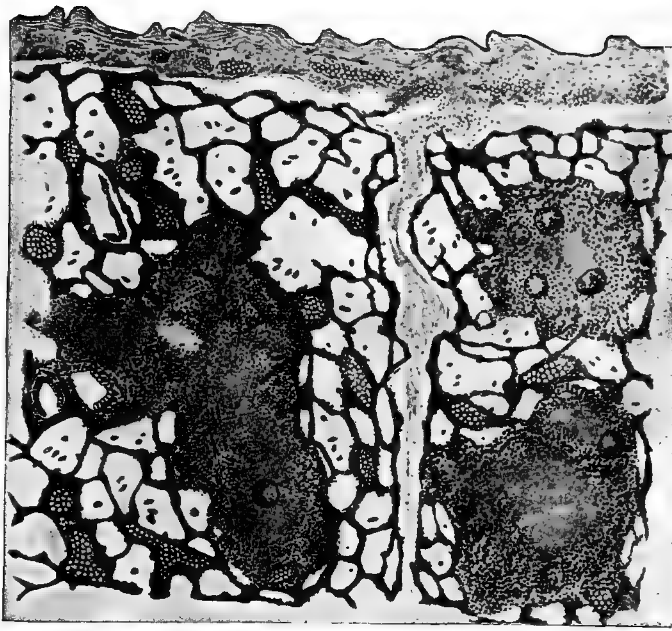



DIAGRAM OF TUBERCLE. (*Coplin.*)

are also giant cells, which occupy the central zone, round or oval, sometimes with processes, containing 20-100 oval or round nuclei, which in old giant cells are arranged in a chain about the periphery; external to these elements there is often a zone of lymphocytes, especially in acute forms of tuberculosis. In chronic cases the center of the tubercle regularly undergoes cheesy (caseous) degeneration, becoming dry, not staining, with coarse or fine granules scattered throughout, or the con-

tents may be softer and creamy, and about the tubercle there may be a new formation of connective tissue shutting it off from the other tissues, with calcification of the fibrous capsule. Or new fibrous tissue in strands may be distributed through the tissue, enclosing tubercles here and there, or in bones and joints

FIG. 76.



MILIARY TUBERCLES IN THE LUNG OF A CHILD. (*Birch-Hirschfeld.*)

Thickened visceral pleura above. Three tubercular masses containing giant cells, caseous in the middle portions, non-vascular, surrounded by aërated vesicles with vessels in their septa.

the formation may be spongy and fungus-like. On mucous membranes there may be warty or papillary growths as also in the skin (usually known as lupus). The giant cells and the epithelial elements may come from the lymph-vessel endothe-

lium, the adventitia of small blood-vessels, from fibro-blasts, or from leucocytes which wander into the tissue in response to the products of the bacilli (cytotaxis). Carried elsewhere from such a focus the bacilli often cause capillary thrombi and new tubercles develop from these. Imperfect vascular supply is

Fig. 77.

Tuberculosis of the Skin. (Photo.)
Tuberculosis verrucosa cutis.

constant in tubercles. Beside distribution through the vessels, often after the wall of a vein is attacked, the lymph stream is commonly involved and adjacent nodes soften and are caseous. Bacilli taken into the mouth may reach the lymph channels by entrance into the tonsils and set up a reaction in a nearby

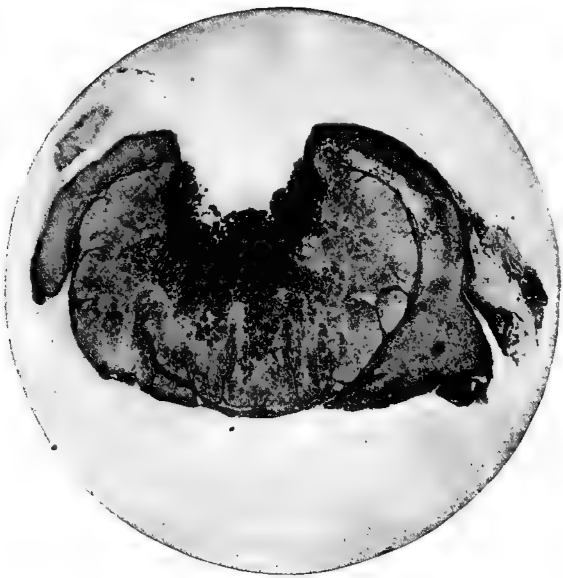
node which protects the system by bursting and discharging superficially. A lung attacked by tubercle becomes more affected, and the disease spreads to the other lung, by inhalation of sputa containing bacilli. By swallowing such sputa the intestines are often diseased, phagocytes taking the bacilli into the lymphoid tissue and thus producing typical fibrosis and ulceration. About 80 per cent. of adult cases have intestinal tuberculosis as well as pulmonary.

The commonest port of entry is the respiratory system, dried sputa containing bacilli being inhaled with street dust. Tuberculosis in the new-born may come from the paternal side (spermatogenous), the maternal (oögenous) or an infected placenta (plakogenous); but the influence of heredity is now considered less important than formerly, all that is inherited being probably a constitution below normal in resisting power. Tubercular disease is estimated to be responsible for at least forty per cent. of all deaths in large cities. In childhood the bones and the lymph nodes are most often the seat of tuberculosis, with affections of the lungs and other organs later; in adult life the lungs are especially attacked though no tissue is exempt. The effect of tuberculosis varies according to the extent of the process and its site, such affections of the nervous system being obviously more important than a local nodule of lupus in the skin. Generally distributed through all the organs in an acute attack tuberculosis is often rapidly fatal; as an encapsulated focus in the apex of one lung, it deserves the name "latent" and may exist for years without causing symptoms. When serious in its effect it is partly by the toxins of the tubercle bacilli and partly by those of associated organisms (as pyogenic), which latter explain the night sweats, fever and emaciation observed in pulmonary consumption. The source of human tuberculosis may be some of the lower animals, many other vertebrates suffering from it (cow, horse, pig, dog, cat, rabbit, monkey, chicken, dove, parrot, etc.).

**Actinomycosis.**—Commonly found in cow and horse, per-

haps derived from spores among grain, may gain entrance to the human system by way of decayed teeth or by inhalation. Wherever lodged the fungus forms a hard nodule, which increases in size, softens and discharges purulent fluid, containing small yellowish points, which under the microscope show the

FIG. 78.



MOLLUSCUM CONTAGIOSUM. (PHOTO.)

Above the skin surface and the ulcer, discharging "molluscum bodies." Below the main body of the tumor inverting the skin.

characteristic rayed appearance. By invading blood-vessels, metastatic deposits in liver, brain and other organs occur. Often there is but one focus, and that of slow and chronic course, and by proliferation of fibrous tissues it may be encapsuled and healed. The disease is not common in man and is an

occupation disease, usually affecting those who handle cattle — butchers, etc.

**Molluscum contagiosum** is a disease of the skin, appearing often in small epidemics, evidently due to inoculation by a parasite. The skin presents one or more papular or warty nodules, from 3 to (later) 10 mm. or more diameter, with a softened cheesy center, usually on the face or trunk. Under low magnifying powers an invagination of the skin is found, about a hair-follicle as its axis, crowded with degenerated cells and small oval molluscum bodies, which may be intra- or extra-cellular. The epithelial cells are apt to become horny. Similar bodies are found in the muscles of sheep, pigs and other animals, and are known as Miescher's sacs, Rainey's bodies, and are grouped under the head of sarcosporidia.

**Mycosis Fungoides.**—Among the rarer infectious diseases, of which the cause has not been found, but probably due to a protozoan parasite. It begins as a patch of eczematous reddening anywhere on the body surface; nodules then develop of varying size but may be 8 to 10 cm. in diameter; the summit of the tumor softens and discharges clear or blood-stained fluid and the whole appearance of the growth resembles a tomato, red and fungous. Under the microscope there is a profuse development of new connective tissue about the vessels and papillæ, infiltrated with lymphocytes, with mast cells, giant and epithelioid elements; pus cells are found only at late stages; vascular supply is scant and hence the tendency to necrosis.

**Madura foot, mycetoma,** is a chronic process attacking the extremities in two forms, the pale or ochroid and the melanoid; rapid growth of granulation tissue with necrotic changes, formation of sinuses and discharge of little spherules like the globules of caviar ("fish roe"), which are black in the latter form and yellow or brown in the former. These may be cultivated in usual media and resemble actinomycosis fungi, but clinically the disease differs in being confined to the hand and foot in tropical countries and without metastasis.

# CHAPTER XI.

## METHODS.

### A. Post-Mortem Examination.

A CADAVER is examined for the purpose of determining the cause and manner of death, but most often what we find is a series of anatomical changes in the organs, which we must then interpret, giving to each its relative value and deciding as well as may be which of several diseases probably determined death. If the case is one of legal importance the body should be identified, all distinguishing marks, scars, moles and deformities noted, with the weight, color of eyes and hair, number of teeth present and any gold or other fillings, and especially any external signs of violence. It is important here to distinguish injuries happening before death and those which may have occured afterward. The main difference is that the ante-mortem wound presents evidence of bleeding, gapes if incised or torn, with beginning efforts at repair or evidence of inflammation, while post-mortem blows (later than two hours after death) do not usually produce ecchymosis, nor will incisions be followed by bleeding, and inflammatory and reparative changes are absent; microscopical examination may be required to decide the question. The first stages of decay often simulate ante-mortem lesions and must be recognized and separated from effects of disease (see pp. 94-95).

The post-mortem examination is divided into inspection of the exterior, section and examination of the various organs in a regular order and the summing up or gross anatomical diagnosis, to be followed by microscopical examination of the chief organs

after hardening and section. The clinical history of the case should always be read before beginning the autopsy, and the findings of the latter kept with a copy of the former. As the autopsy progresses the findings in each organ, with its weight, should be dictated to a scribe, and the whole signed by the pathologist, the microscopic examination added later.

## External Inspection.

Weight of body; height measured between uprights as the body lies on the back; distinguishnig marks, teeth, and wax cast of mouth if necessary; presence of decomposition as greenish hue of abdomen and prominence of superficial veins from imbibition of blood coloring matter; evidence of fractures, etc.; venereal scars and warts; presence of edema of ankles, scrotum, labia, ascites; post-mortem lividity, rigor mortis; skin lesions, tattoo marks; probable age of individual. If only part of a body is present, as head and upper extremities, twice the length of the arm, from the mid-sternal line to the tip of the middle finger (measured along the flexor surface in abduction), or the distance between the tips of the middle fingers along the flexor surface, the arms extended at right angles to the main axis; or, if but one extremity be present, twice the length measured from the glenoid cavity plus half the distance between the glenoids, meâsured between perpendicular lines, or nineteen times the length of the middle finger, will give the approximate height. The distance from the tip of the olecranon to the tip of the middle finger is about five-nineteenths of the height. The upper border of the symphysis in the adult is said to mark the mid-point of adult height, but this is not trustworthy, especially for women. From the head of the femur to the plantar surface of the heel is half the height, and the length of the femur alone is one-quarter of it. As many of these measurements as possible should be taken when necessary. Such estimates of the height and size of the total body may be of vast

medico-legal importance (see tables of weights and measures, p. 308).

## Internal Inspection.

**Head and Brain.**—Make incision from tip of one mastoid process over vertex to the tip of the other. If the head is bald carry the top of the incision a little farther backward; in any case cut through to the bone, strip up periosteum and scalp either side of the cut till two flaps are formed, reflect one over the face and the other backward. Leave the temporal muscles for sewing, but cut through them with a knife where the saw cut is to come. Begin the saw cut with the saw at right angles to the main axis of the skull at a point 3 cm. above the glabella, steady the blade against the thumb of the other hand, *pull* the saw till a good mark is made, cut with the thrust on a horizantal circumference on one side to 5 cm. above the mastoid tip, repeat on the other side, taking care not to go through dura. By a posterior saw cut running from one end to the other of the former line and about 3 cm. above the external occipital protuberance, complete the separation of the skull. The bone is thick at four points, in the mid line front and back and over either mastoid; at other points it is thin, especially in the temporal fossæ; a gentle blow with a chisel at one or more of these points may be needed. Then insert the blade of a strong forceps in the mid anterior cut and twist, then the jaws of the forceps and pull off the calvaria; if the dura is too adherent it may be taken along, or separated from the bone by a long blunt instrument. If dura and bone be not removed together, cut the membrane carefully from within outward along the saw cut; run a slender knife along the process to the crista galli and cut transversely, putting the dura on tension; strip it back from the vertex with slight touches of the knife over the pacchionian bodies. Note its blood content, presence of inflammatory exudates or blood on either surface, tumors, etc., slit up the superior longitudinal sinus and note the clot.

The pia is now exposed — note the blood content, presence of edema below or in its meshes, thickenings, pus, tubercles.

Gently lift up the frontal lobes and elevate the first nerves, cut from behind forward through the optic chiasm, then the internal carotid of each side, always repeating on one side the incision done on the other and *using little force.* Run the knife, from below and within, out and back along the petrosal ridge, cutting the tentorium; then divide the other nerves in order; then the vertebral arteries from behind forward and as low as possible. Reach the scalpel with the blade forward down by the side of the medulla, rest the handle on the basal process as a fulcrum, turn the blade transversely, carry the handle toward the forehead which carries the blade back, cut the medulla as low as possible with a single clean sweep. Drop the knife, support the vertex with one hand covered with a towel, reach in two fingers either side of the medulla and with a rotating motion about a transverse horizontal axis lift the cerebellar lobes out and up.

Lay the brain on its vertex on a towel or in a pan of water and examine the base. Note the arteries, size, malformations, presence of atheroma, tubercles, follow them into the Sylvian fissures where sometimes tubercles are found when absent elsewhere and emboli and hemorrhage are common.

Turn the brain on its base, separate the hemispheres, cut into a lateral ventricle along a line starting in the gray matter just anterior to the corpus callosum, running through the outer margin of the corpus backward into the convolutions over the posterior horn of the ventricle. The knife is held at 45 degrees in the first third of the cut, more nearly horizontal in the middle third, and at 45 degrees in the last third. The roof of the ventricle is usually opened in the mid-third posteriorly and may be completely opened by cutting from within out into each horn; repeat on the other side. Lift up the anterior portion of the corpus callosum and dissect it backward off the velum and choroid plexus, cutting through the foramen of Monro upward,

and behind sever one of the posterior limbs of the fornix and reflect to the side. With the pons and medulla supported on two fingers, cut through the vermiform process into the fourth ventricle, continue into the aqueduct and the entire ventricular system is exposed.

Make a series of anterio-posterior wedges through each hemisphere, just external to the ganglia at the base, the thin edges of these coinciding. Or make a cut just outside of the great ganglia from before backward to the pia, open the cut surface outward and make another at right angles to the first, another at right angles to this, always unfolding, and another. Or make a series of sections of the entire brain running transversely across the main axis from above downward and before backward, better after hardening in Müllers' fluid. The cerebellum is opened along the tree and by a series of cuts at right angles through each half. Lastly a series of transverse cuts through the ganglia, supporting them from below. The brain is then folded together again, turned over, and the pons and medulla sectioned transversely while supported by a finger or two below, the cuts placed close together.

This method, though the one usually seen at necropsies, is essentially crude and many of the relations of different parts entirely destroyed; for fine work the entire brain should be hardened in alcohol or Müller's fluid or formalin solution before cutting. All cuts above given should go to the pia but not include it, and should be made with one firm stroke, the knife acting like a microtome knife and wet with water between each two sections. Then no matter how much the original appearance of the organ is changed by the process, it may be restored by folding together and lesions localized by referring them to the chief fissures and convolutions, because the wedges of brain tissue are held together by the pia.

After examining the brain, break through the roof of the middle ear and of the orbits and examine the contents of each; if the eye is wanted for further examination, it may be cut just

behind the conjunctival margin and removed, the anterior half left in situ and stuffed slightly with cotton. Some of the great ganglia of the skull are easy of access, especially the Gasserian, lying on the point of the petrous bone just under the dura mater.

If fractures have been found in the skull the dura should be stripped from the base and the lines of fracture traced before the ear and eye cavities are opened, and chisel and mallet must not be used till the injuries are fully described; in medico-legal cases, not at all.

The spinal cord may be removed either before or after the thorax and abdomen are examined. The body is laid prone, the head hanging over the edge of the table, the abdomen laid on a block of wood to lessen the lumbar curve. An incision is made along the spinous processes, and integument and muscle removed to one side from the lateral spinal groove; repeat on the other side. See that the bottom of the groove is clean, exposing the laminæ, saw through these so as to enter the outer part of the canal but not to injure the cord (about 1 cm. from spinous processes); be sure to sever the laminæ completely with the first sawing. Strike the spinous process on one side with a mallet and then on the other and cutting through the ligaments in the lower lumbar region lift up the freed spines in one long series with a strong forceps. Pick up the dura over the cauda equina with a pair of mouse-toothed forceps and cut the nerves from below upward one side and the other, and with a little care most of the posterior root ganglia can be removed with the cord. Do not handle the cord with any force or allow it to be bent. Lay it on either its front or posterior side and open the dura carefully with a probe-pointed scissors. With a sharp razor make exact transverse cuts through the cord between each two pairs of nerves leaving the segments attached by pia; hang the cord in a tall jar of Müller's fluid with a light weight at the lower end till hard enough to cut. Examine the vertebræ for dislocations, etc. After the trunk viscera have been removed

the spinal canal may be opened from the anterior aspect by means of a strong curved chisel, but the results are not so satisfactory as by the other method.

**Thorax and Abdomen.**— Body on its back, long single incision from 3 cm. above episternal notch to pubes, going to the left of the umbilicus, the knife held in the whole hand with the wrist firm, the movement taking place chiefly at the shoulder joint. *Do not make any cuts with the index finger on the back of the knife!* As the first cut opens the abdomen, usually in the upper zone, a finger may be hooked into the cut and the abdominal wall lifted strongly toward the operator and the incision completed, the knife inserted external to the peritoneum just over the pubes and the tendon of the rectus abdominis severed from within out.

Then hook the thumb under the abdominal flap nearest, spread the fingers on the thorax, press with fingers and pull with thumb to make the free edge of the costal cartilages prominent, and cut along their margin. Grasp the integument and muscles over the thorax firmly, pull strongly toward you, and sweep the thoracic wall clean with long cuts of the entire blade; repeat on the other side. Lay the knife down and inspect the abdomen, *not touching anything, merely looking;* note the position of the organs, presence of fluid and character, and catch what runs off for measurement; then lift up the omentum, remove it, and examine the coils of intestine. The normal peritoneum is shiny like all serous membranes and transparent.

With the palm upward reach under the ribs and determine the height of the diaphragm on each side in the mid-clavicular line, usually about the fourth rib or space on the right side, and a rib or space lower on the left; if unusually low it points to fluid or increased volume of organs in the thorax. If pneumothorax is suspected, hold the skin and muscle flap of the thorax up and fill the groove next the ribs with water, puncture a space below the level of the water and note bubbles issuing

from thorax. Or water may be put in the upper abdomen and the diaphragm punctured.

Now cut the costal cartilages from the second down, sweeping lightly outward to the ninth, resting the knife on the following one of each pair before the former is quite cut through, holding the knife as horizontal as possible, to avoid cutting the lung. Lift the sternum by the xiphoid cartilage, transfix the attachment of diaphragm so that the knife comes out in the line of section of the cartilages and cut away from the xiphoid and out, repeat on the other side. Now grasping the end of the cut cartilages on one side lift the sternum strongly upward and dissect it from the thoracic contents by long transverse sweeps of the knife, keeping close to the bone to avoid opening the pericardium. When this is complete as far as the first rib the knife should be carried out toward the shoulder about 4-6 cm. and the cartilage of this rib cut upward on each side. Disarticulate the clavicle by running a slender knife along the line of the joint, entering it from the episternal notch, curving down and out, *holding the handle of the knife nearer the subject's chin than the blade* because the plane of the joint slants and a perpendicular knife meets sternum above and clavicle below. This is often one of the hardest points for a beginner in making autopsies, but if the plane of the joint be kept in mind and the knife slanted properly it follows the joint without the need of any great force. The sternum being practically freed from all its attachments should be *twisted out* rather than cut, to avoid escape of blood from the large veins of the neck into the thorax.

The lungs and heart are exposed; note how nearly the former approach in the median line, normally they touch at the second rib. Note adhesions in the thorax, measure fluid. Open the pericardium by picking up a fold and incising transversely; air rushes in and the point of the knife is then carried down to the apex, up to the base, and over to the right from about the middle of the main cut, always from within out. Note the con-

dition of the pericardium and its contents; measure the latter if abundant. Feel the great vessels for aneurysm.

Grasp the heart by the base and turn it up to expose the posterior surface. Estimate by the eye a line midway between the anterior and posterior coronary arteries and along this cut into the left ventricle from the base to the apex with one long sweep of the knife. Open the right ventricle by a similar cut midway between the posterior coronary and the right (really the inferior) margin of the heart, the space being usually quite free from fat. As the left ventricle is opened insert the index finger of the left hand, put the thumb into the other cut — between the two is the septum -- and with that hold the heart is easily managed in the further cutting; avoid pressing the septum between thumb and finger. Lift the organ straight up and cut the stretched vena cava inferior as long as possible just as it enters the pericardium. Swing the heart to the right side and cut the pulmonary veins on the other, reverse and cut the remaining pulmonary veins and superior cava. Only the aorta holds it now and that is cut from below upward as the heart is lifted and carried toward the chin; if the knife is sharp and clean long cuts are made, two or three are enough and there is no spattering of blood.

Lay the heart on its front. Having kept the original hold the inferior vena cava is above the thumb; enter it with the probe end of the enterotome and come out the superior, and then with a single cut open the right auricle, turn out the clots. Reverse the scissors, enter the probe blade from above through the tricuspid valve and out of the first knife cut and thus open the ventricle. On the anterior flap of the right ventricle, thus formed, look for a papillary muscle, pass the probe blade in front of this and cut on the anterior wall across to the pulmonary valve, aiming for a small pledget of fat on the infero-anterior aspect of the pulmonary conus and thus cutting into the artery between the cusps of the valve. Open the left auricle by cutting from one pulmonary vein to another; run the probe

blade from above through the mitral and bring it out of the first cut, thus cutting through the external flap of the mitral. Now turn the apex of the heart toward you, pass the probe blade behind the internal flap of the mitral and on the anterior surface cut from apex along coronary artery *but not across it* to the appendix auriculæ. Stop cutting and push the probe blade out of the aorta, rotate the hand outward (supinate) about fifteen degrees and cut into the aorta, drawing the pulmonary artery out of the way with the left hand. Thus the entire inner suface of the heart with its four valves is exposed by two cuts in each auricle and two in each ventricle, of which latter the first is made on the posterior surface of the ventricle before the heart is taken out, and the second on the anterior surface after removal. Wash out clots, weigh the heart, measure its walls, estimate the capacity of each chamber, note the condition of the valves and the muscles, examine the arch of the aorta for atheroma, slit up one or both coronaries.

The competency of the cardiac valves can be better determined by careful inspection than by passing two or more fingers into them while uncut and estimating their size by the degree of separation possible between the fingers, and so-called hydrostatic tests are equally untrustworthy.

The lungs may be removed by grasping each firmly by the apex, drawing it horizontally toward the symphysis, thus making the structures at its root tense, and cutting across them, or by lifting one out of the chest till it rests on the ribs and then cutting across the bronchi and vessels. Usually both are removed before either is studied. They can be referred to the proper side by remembering that the posterior border of each is rounded, the anterior margin thin, the base a shallow cup to correspond with the diaphragm, and the bronchi, etc., on the inner aspect. Set the organ on its base, the apex is at once evident and the borders determine its relation in the body; the right lung has three lobes normally and the left but two, but variations are common. Note the condition of the pleura;

if firm old adhesions are present it may be necessary to make an incision in the costal pleura and strip it from the inner side of the ribs, removing both layers with the lung. Open the large bronchi with a probe-pointed scissors, and the vessels likewise. Lay the lung on its inner surface and make a single long cut through its rounded posterior margin from apex to base and from pleura to hilum. The object of such long smooth cuts is to secure a smooth even surface for inspection, and they require and repay careful practice. Note the relative air and blood contents of the lung, its solidity, color, smoothness of section, density and friability on gentle pressure with the finger; cut off a shaving from the most solid part and see if it floats in water. Weigh each lung.

With the enterotome cut the diaphragm on each side of the middle line back to the spine and rotate the liver upward into the thorax, to gain more space for the abdominal organs.

Remove the spleen by gently drawing it toward the middle line and cutting from above downward across its hilum on the external aspect. Note its size, weight, conformation, condition of capsule, presence of infarcts; make a single long cut through it and note the lymphoid elements, proportion of fibrous tissue, consistency of the organ as a whole; if waxy, test for amyloid changes.

The omentum may be removed after inspection when first reflected after the abdomen is opened or at a later stage. It is well now to lift up the small intestine near the cecum, cut through the mesentery and then gently pulling on the gut with one hand, keep drawing a sharp knife across the mesentery like a violin bow, close to the gut, cutting only mesentery but doing that thoroughly, keeping the knife nearly flat, putting the intestine into a special pan as taken out. Cutting thus from below upward, when the duodenum is reached it is ligated and cut distal to the ligature. The stump of the mesentery is then removed. The large intestine is removed by drawing the cecum toward the middle line, cutting the peritoneum externally, lift-

ing the gut up and toward the opposite side and dissecting it off subjacent structures, being careful not to wound either the right kidney or the duodenum. It is then separated along the transverse portion from the stomach and from the splenic flexure downward to the rectum, which is tied and cut; or, more conveniently often, from rectum to splenic flexure as on the right side, from below up. The entire gut is now opened separately in the sink, washed and studied, the small intestine being cut along the mesenteric attachment and, if necessary, the contents of each portion is caught in a separate basin for further examination.

The kidneys are now removed with the adrenals, either by making a superficial cut across the hilum of the organ through the peritoneum, inserting two fingers of each hand and shelling the organ out of its fatty capsule, or by cutting on the outer aspect, drawing the organ across the spinal column and taking the fatty capsule with it. In either case it is well to cut the vessels from above downward and when free from them, by gently pulling to disclose and examine the upper portion of the ureter. If necessary the urinary tract may be removed entire, and in that case the ureters are dissected down to the bladder, and with the attached kidneys turned downward till the pelvic organs are removed. Each kidney should be freed from its proper capsule by a very superficial incision through it along the convexity of the organ, which permits it to be stripped off, the inner side of the capsule examined, as also the surface of the organ, to see if kidney tissue is torn off with the capsule. The color, blood content and smoothness of the kidney surface are noted and cysts and infarcts described. A long incision is made through the convexity of the organ down to the pelvis, opening it; the capsule and fatty tissue tucked between the middle and ring fingers of the left hand allow complete control of the organ while this cut is being made. The relative proportion between cortex and medulla is noted, color of cut surface, presence of fat and urinary salts in the tubes, prominence of

the glomeruli in active hyperemia, increase of connective tissue, state of the pelvic mucous membrane, capacity of the same, etc.; weight of kidneys. If waxy test for amyloid.

The liver is grasped by the left hand, the fingers behind and over the convexity, the thumb in the anterior notch, and the organ thus firmly held is lifted while its attachments are cut, the knife laid aside for a moment while the portal vein and common bile duct are palpated. Without changing the hold described the organ is lifted and freed, then weighed, and examined externally; one or several long anterior cuts across both right and left lobes are made and the blood content, amount of connective tissue, bile staining and the presence of fat determined. If waxy test for amyloid.

The ligatured end of the duodenum is now lifted and it is removed from below upward with stomach and pancreas. The stomach is opened from above along its greater curvature and into the duodenum, its contents caught in a clean pan for examination, the condition of the mucous membrane noted. The stomach may also be opened the first thing after the thoracic organs, by splitting the upper third of the duodenum and cutting along the greater curvature. Gentle pressure along the course of the common bile duct causes bile to exude, or, if not, a probe can be inserted as far as it will go and the duct traced out while the relations of the liver are unchanged. A series of transverse cuts along the entire length of the pancreas is made and the cut sections examined; small points of fat necrosis should be looked for, and the pancreatic duct opened and traced.

When the organs in the neck are examined the knife is swept within the ring of the two clavicles close to the bone, the tissues under the skin on the front of the neck dissected free as far as the hyoid body and from here to the symphysis. The knife is then pushed through the floor of the mouth directly behind the symphysis and swept on each side back and out close to the inner surface of the lower jaw as far as the angle; and from here back and in to the vertebral column. Then the trachea

and esophagus are elevated toward the chin and the dissection carried up behind them as far as opposite the roof of the mouth. The tongue is then drawn downward, the lateral pillars of the fauces and the soft palate severed and the entire group of structures removed. The esophagus is opened on its posterior aspect from the pharynx down, then pulled to one side while the trachea and posterior wall of the larynx are opened with scissors.

The pelvic organs are removed together by cutting through the peritoneum along the brim of the pelvis and by blunt dissection separating it from the inner pelvic aspect as far as possible. Then the cut and tied end of the rectum is grasped and pulled strongly up and toward the symphysis pubis while dissection is carried on behind it. The pelvic contents are now attached only around the margins of orifices leading out of the cavity, and by traction on rectum and bladder together these attachments are made tense and cut across.

The rectum is then opened on its posterior aspect and examined. A notch is made in the vertex of the bladder with the enterotome and the cut made on the anterior wall, the probe-point passing out of the meatus internus. The uterus may be opened on either the anterior or the posterior surface, preferably the latter, by a sharp knife, just cutting into the cavity. Section into the vagina is completed with scissors *from above downward;* in this way the pathologist knows that if anything is found in the uterus he did not carry it up from the vagina on the point of his scissors, a matter of importance in medico-legal inquiries. Secondary cuts open the cornua and display the entrance of the tubes. A single long cut in each ovary is usually enough. The testicle may be pushed up to the internal ring and there cut into without mutilation of the external genitals.

In many cases it is desirable now to slit the vena cava inferior and abdominal and thoracic aorta from below upward, and to cut out a portion of a rib and also of one of the long bones.

The calvaria is replaced and held by two stitches in the halves

of the temporal muscle, and the cut in the scalp, as well as the long cut from episternal notch to pubes, closed with waxed white cord in a glover's suture.

Ordinarily a post-mortem examination made as given is adequate for the case studied, or all that is allowed by the friends. The order in which the organs are examined is the usual one and convenient in most cases, but often it is necessary to vary it. In medico-legal inquiries it is of the utmost importance to make a complete and accurate record, with measurements and weights, a photograph of the body and of important injuries, chemical examination of stomach and intestinal contents, and careful distinction between what was pathological in the various organs, what was due merely to post-mortem decomposition and what the pathologist was obliged to do in order to examine the parts.

The following may be taken as a fair sample of an autopsy record in ordinary routine hospital work and no less than this should ever be included in the pathologist's report.

RECORD OF AN AUTOPSY ON THE BODY OF

John ———, aged 35, German, married, carpenter. Residence or hospital ward ——.

Died January 1, 1901, 11:30 P. M.

Autopsy January 2, 1901, 2:00 P. M.

Clinical diagnosis — pyemia.

**Inspection.**—Body well nourished, height five feet seven inches, rigor mortis well marked in lower extremities, absent in arms, blue anchor tattooed on left forearm. Incised wound on left leg, upper third, external aspect, 12 cm. long, edges everted and colored green to black, surface partly granulating and partly covered with thin pus and necrotic tissue, odor foul. Abscess cavity in left groin about as large as a hen's egg, apparently opened by incision, no evidence of healing. Tissues of left thigh edematous. Right knee swollen and distended with pus.

**Peritoneal Cavity.**—Small collection of pus localized between spleen and ribs, communicating with small abscess cavity in spleen, shut off from general peritoneum by recent adhesions.

**Diaphragm.**—Right side fifth rib, left side fifth space.

**Thorax.**—Small amount of turbid serum in right pleural cavity, no adhesions either side.

Pericardium normal. Heart weighs 360 grams, muscular tissue pale and soft, valves competent, small recent vegetations on mitral and aortic valves with subendocardial hemorrhages in the neighborhood, vegetations on ventricular aspect of each valve, easily detached.

Right lung presents an area of red hepatization on posterior third of lower lobe, remaining portions congested and edematous, bronchial mucous membrane congested and covered with muco-pus.

Left lung contains several small foci of pus in both lobes, the largest about the size of a hazel nut, with a zone of red hepatization about each; dependent portions congested, whole lung edematous. A small area of caseous material in the apex walled about with firm fibrous tissue. Bronchi as above.

**Abdomen.**—*Spleen* large, soft, weighs 340 grams, presents an abscess cavity on outer aspect which communicates with a collection of pus as described above. The rest of the organ very congested.

*Kidneys,* weight together 375 grams. In each the capsule is not adherent, surface smooth with dark mottlings, cortex swollen, its markings very indistinct, pyramids darker in color, pelvic membrane normal.

*Intestines.*—Small intestine normal; large intestine shows some edema of mucous membrane, solitary follicles prominent and here and there ulcerated and surrounded by zones of hyperemia.

*Liver.*—Weight 2,560 grams, the acini contain much fat in their peripheries. Gall-bladder contains one small calculus; bile normal.

*Pancreas* apparently normal.

Pelvic organs normal.

**Head.** *Brain.*—Dura normal. In the meshes of the pia over the vertex, between the convolutions and at the base, especially along the Sylvian fissure, there is pus in appreciable quantities.

Spinal cord not examined.

*Veins.*—Partly softened thromboses in left external iliac vein just above Poupart's ligament, loosely attached to the vein wall, about 5 cm. long, color reddish.

Gross anatomical diagnosis; pyemia, malignant endocarditis, meningitis.

A——— B———, M. D.

Space for histological and bacteriological report.

## B. Disposition of Material; Preservation; Hardening.

Fresh material gathered at the autopsy may be immediately cut by the freezing microtome and the sections examined, but as a rule all tissue has to be put through various processes to fit it for microscopical study. The tissue elements must be fixed in the position and condition sustained during life, hence it is important to gather material in as fresh a state as possible, and they must also be nardened to resist the various stains and dehydrating fluids with which they are treated later. Often the same fluid accomplishes both results, fixing the cells, hardening the tissues and also producing optical differences, which aid further study, and as a rule the best fixatives are mixtures with an acid reaction. They vary much in power to penetrate tissue and hence for some fluids the material must be cut into small pieces and exposed to a great bulk of fixative. Heating the material in the fluid increases penetration. After fixing, the tissue must be thoroughly washed to remove the fixative, or staining will be imperfect. Tissues hardened in bichloride of mercury, chromic acid and chromate solutions may be washed out with water; picric acid and its compounds require alcohol and heat facilitates the process.

**Fresh Material.** *Fluids.*—Put a drop on a slide, cover

quickly and examine with a half inch and then with a sixth; if rich in cells, thin with normal salt solution (0.6 of one per cent.). A little vaseline along the cover-glass will prevent too rapid drying. If the fluid is poor in cells, sediment in the centrifuge. If desired to keep the fluid for a time, make a hanging drop over a hollow slide and ring with vaseline. Tissues may be scraped over a smooth cut surface and the material so obtained examined as above. A little of such fluid may be taken on the end of a slide and drawn smoothly over another and the film on the second slide studied before or after drying and staining. Elements may be fixed on the slide by coating it first with white of egg and glycerine, or by gentle heat over a Bunsen burner after the spread is dried in the air.

Tissues often require to be thoroughly teased in normal salt solution, glycerin, hydrocele or ascites fluid, and sometimes it is well to soften the tissue first to loosen the attachment of cells to basement substance; this is called maceration and the fluids most used for the purpose are:

1. Alcohol, 33 per cent. (Ranvier's). Soak the tissue 24 hours in small pieces; good for muscle and gland tissue.
2. Freshly made potassium hydrate solution, up to 32 per cent., which is very rapid, 10 to 15 minutes; tease in the solution, not in water; to preserve the specimen, take it from the potassium solution and put it into 50 per cent. acetic acid, wash thoroughly, then wash in water, mount in glycerin after staining with alum carmine. Good for smooth muscle and tissues containing it.
3. Chromic acid and its salts (acid 1 to 20,000; Müller's fluid or 2 per cent. potassium bichromate) leave in the former 24 hours, in the latter 2 to

5 days; good for nervous tissue, ganglion cells, etc.

4. Osmic acid, 1 per cent. solution, for nerves.

To clear up certain details it is well to treat fresh material with various chemical fluids, and they may be allowed to flow under the cover-glass if a drop is put on one side and a small piece of blotting paper on the other:

1. Acetic acid swells connective tissue and cell protoplasm and renders them transparent, shrivels nuclei and makes them prominent, precipitates mucin, distinguishes between fatty and albuminous granules by promptly dissolving the latter, elastic elements and parasites not influenced and hence allowed to become prominent; may be used pure (glacial acetic) or in various dilutions, 2 to 5 per cent. best.
2. Potassium acetate, saturated solution in water; clears, and makes nuclei prominent.
3. Potassium and sodium hydrate solutions, 1 to 3 per cent., dissolve most tissues, leave elastic, fat, pigment, amyloid, bone and bacteria untouched. Macerate if strong.
4. Hydrochloric acid, 3 to 5 per cent. dissolves osseous tissue with production of $CO_2$ bubbles. Dilute sulphuric acid also dissolves bone and crystals of calcium sulphate form.
5. Osmic acid, 1 to 2 per cent., colors fat black.
6. Dilute iodine solution, best in the following:

| | |
|---|---|
| Iodine, | 1.0 |
| Potassium iodide, | 1.0 |
| Distilled water, | 100.0 |

Mix; dilute with 3 to 5 parts water for use; this renders nuclei and cell contours distinct and colors glycogen and amyloid brown.

7. Staining solutions of various kinds may be drifted under the cover-glass in the same way and the excess washed out with distilled water.

## Fixation and Hardening.

General rules —

Cut the tissue into cubes not larger than 1 cm. on each edge.

Use 10-20 times as much fluid, bulk for bulk, and change if it grows turbid.

Put a layer of absorbent cotton or filter paper in the bottom of the jar, that the fluid may act from all sides and discoloration by precipitates be avoided.

After the tissue is hard enough, wash 12-24 hours in running or frequently changed water and then put into graded alcohols, 70, 80 and 90 per cent., each for 24 hours.

Usual fluids for this purpose are:

### I. Alcohol.

Ninety per cent. to absolute alcohol, changed every 6-8 hours for three times; preserve in 90-95 per cent. Good for rapid work and where bacteria are suspected in the tissue; also, if substances present, as glycogen, which are soluble in water. After preliminary hardening by other methods, graded alcohols are used, beginning with 70 per cent. This method is not so much used as formerly, because of the shrinking in the preparation and destruction of red cells and pigments. Ordinary " abso-

lute" alcohol of commerce is seldom more than 95 per cent. To remove the remaining water, heat copper sulphate crystals till the water of crystallization is driven off and most of the color is lost, pulverize and add this in at least the proportion of one-third to the alcohol bottle. Repeat the process when the copper salt begins to turn blue; filter the alcohol before use.

## II Formalin.

To an increasing extent this agent has taken the place of alcohol, being satisfactory for both animal and vegetable tissues and preserving the natural color more than alcohol. Formalin of commerce is a solution of formaldehyd in water, about 40 per cent., and the usual dilution used for hardening is 5 per cent. for 12-24 hours, 2 per cent. for two or three days, or, for rapid work, as high as 50 per cent., for half an hour to an hour. The weak solution is usually to be preferred, since with the stronger a precipitate may occur wherever there are red blood cells. It preserves these cells intact, stops the further development of bacteria at once, penetrates well, causes no shrinking and does not injure the tissue if left for a long time. Combinations with other fluids are often valuable, as Orth's mixture of Müller's fluid with 10 per cent. formalin, usually made fresh, good for about four days after making, hardens in 3 to 12 hours; wash well in running water afterward. Formalin may be kept in dark glass bottles, as paraform is apt to precipitate under the influence of light; if this happens a small addition of water and heating redissolve it. Strong formalin is irritating to eyes and hands.

## III. Corrosive Sublimate Solution.

This has so little penetrating power that the pieces of tissue must be very thin and shrinking may occur, but it fixes cells

and karyokinetic figures and preserves red cells and pigment. It is used as

1. Concentrated aqueous solution, 3-6 hours.
2. Normal salt solution saturated with bichloride by the aid of heat (about 7 per cent.); 3-6 hours.
3. Acetic sublimate solution:

| | |
|---|---|
| Glacial acetic acid, | 1 part. |
| Corrosive sublimate, | 3 parts. |
| Distilled water, | 100 parts. |

Leave tissue about twenty-four hours; does not shrivel.

4. Zenker's fluid:

| | |
|---|---|
| Sodium sulphate, | 1.0 |
| Potassium bichromate, | 2.5 |
| Corrosive sublimate, | 5.0 |
| Distilled water, | 100.0 |

Make solution by the aid of heat; just before using add

| | |
|---|---|
| Glacial acetic acid, | 5.0 |

Use about 24 hours; as after all the others, wash thoroughly in water and carry through graded alcohols.

## IV. Chromic Acid and Solutions.

Solutions in water of 0.05-0.5 per cent. for 24 hours to several days, changed daily, penetrates slowly, makes staining uncertain; hence almost discarded for chromate salts. Harden afterward with alcohols in the dark.

1. Müller's fluid:

| | |
|---|---|
| Potassium bichromate, | 2.5 |
| Sodium sulphate, | 1.0 |
| Distilled water, | 100.0 |

Use in large amounts with daily changes for the first week; then every two or three days, then every week, for ten weeks; add a small lump of camphor to prevent formation of mold. The process may be shortened by setting the preparation in the thermostat at 37°-39° C., changing the fluid daily; two weeks enough. Tissues when hard may be cut at once by the freezing microtome or carried through alcohols and embedded; they must be well washed in water and hardened in alcohol in the dark. The sections stain well with hematoxylin-eosin and some carmin stains. Müller's fluid preserves red cells and gives a good section with paraffin imbedding, but it does not stop the action of bacteria in the tissues for some time, injures nuclear structure, and stains the tissue dark yellow. For nervous tissue a mixture with formalin is advisable, as

2.

| | |
|---|---|
| Commercial formalin, | 10.0 |
| Müller's fluid, | 100.0 |

After a time the tissue becomes brittle in this mixture. Formalin may be used alone first and then the Müller's fluid. Make fresh for use.

3. Erlicki's fluid:

| | |
|---|---|
| Potassium bichromate, | 2.5 |
| Copper sulphate, | 0.5 |
| Distilled water, | 100.0 |

Hardens in 8-10 days, but the tissue often shows precipitates.

## V. Osmic Acid and Mixtures.

Make always with freshly distilled water and keep in glass-stoppered bottles in the dark; use small pieces of tissue (1-2 mm. thick) and stir them frequently; fix in the dark, epecially with osmic acid; wash well afterward. Imbed in paraffin, not in celloidin, because ether dissolves out the fat stained black by the acid, and use chloroform or clove oil, xylol also dissolves the fat; clear with ethereal oil; mount in thick Canada balsam containing as little xylol as possible, softening it by heat.

1. Pure osmic acid, 1 per cent. solution, after 24 hours wash and harden in alcohol, stain with safranin or toluydin blue.

2. Fleming's mixture:

| | |
|---|---|
| 1 per cent. chromic acid sol., | 15 parts. |
| 2 per cent. osmic acid sol., | 4 parts. |
| Glacial acetic acid, | ½-1 part. |

Tissue left 24 hours, well washed, hardened in graded alcohols; good for karyokinetic figures and structure in general; sections take carbolic fuchsin, gentian violet and safranin well, hematoxylin not so well.

3. Hermann's mixture:

| | |
|---|---|
| 1 per cent. platinum chloride, | 15 parts. |
| 2 per cent. osmic acid, | 4 parts. |
| Glacial acetic acid, | 1 part. |

Thin pieces from 1-4 days, wash 3-12 hours, harden in alcohols; stain with safranin or gen-

tian, good for nuclear and also protoplasmic structure.

4. Altmann's mixture:

| | |
|---|---|
| Potassium bichromate sol., | 5 per cent. |
| Osmic acid, | 2 per cent. |

Mix in equal volumes, leave tissue (*taken immediately after death* and *cut very thin*) 24 hours, wash well, harden in alcohols, imbed in paraffin.

## VI. Cooking.

Small cubes of tissue may be dropped into boiling water for ½ to 1 minute and then carried through graded alcohols; good for edema, especially pulmonary, albuminous exudates, as in kidney, etc.

## VII. Decalcification.

General rules:

Use plenty of fluid; small pieces of tissue, wash thoroughly afterward; in the case of some methods fix well first (see below); imbed in celloidin usually; the tissue is pliable when when decalcified and allows a needle to penetrate it easily.

1. In Müller's fluid: Fix in formalin, leave small pieces several months to a year with daily changes at first; or hasten the process in the thermostat; good for bones of fetus and infant.

2. In picric acid: Fixing not necessary; use saturated aqueous solution several months;

good for small bones, but very slow; to remove the picric acid, wash and lay in alcohol to which twenty to thirty drops of saturated aqueous solution of lithium carbonate have been added, more lithium will be required from time to time till the tissue is pale in color.

3. In hydrochloric acid: Used alone in 3-5 per cent. solution, but injures the tissues and the following are better:

4. Ebner's fluid, aqueous:

| | |
|---|---|
| Sodium chloride sol., saturated, | 100.0 |
| Distilled water, | 100.0 |
| Hydrochloric acid, | 4.0 |

Leave the fixed and hardened osseous tissue till decalcified, adding 1-2 cc. HCl every day or so; wash and put through alcohols.

5. Ebner's fluid, alcoholic:

| | |
|---|---|
| Hydrochloric acid, | 2.5 to 5.0 to 10.0 |
| Alcohol, | 500.0 |
| Distilled water, | 100.0 |
| Sodium chloride, | 2.5 to 5.0 |

Fix beforehand; the more powerful solution hastens the process, which is slow at best.

6. In nitric acid: Thoma's method. Fix and harden; put the tissue in

| | |
|---|---|
| Alcohol, | 5 parts. |
| Nitric acid, | 1 part. |

for two or three weeks; change the fluid frequently; wash in alcohol; remove the acid thoroughly by alcohol to which has been added calcium carbonate in excess.

7. Phloroglucin: Make a stock solution as follows:

| | |
|---|---|
| Nitric acid, C. P., | 10 cc. |
| Phloroglucin, | 1 gm. |

Dissolve carefully; if with the aid of heat, under a hood; then add

| | |
|---|---|
| Distilled water, | 50.0 cc. |
| for use add | |
| Nitric acid, | 10.0 cc. |
| Distilled water, | 50.0 cc. |

This acts very rapidly, 30 minutes to 12 hours according to age and size of bone; wash in water 48 hours.

8. Trichloroacetic acid: Tissue fixed, put in 5 per cent. aqueous solution of the acid, often changed, ready in 5-6 days; results very good usually.

## VIII. Injection.

Lumina, especially of blood-vessels, are often filled with some injecting material. This usually consists of a vehicle and a dye, but the method is seldom required for pathological work and hence but two or three of the common fluids need be mentioned. The most important vehicles contain either glycerin or gelatin; the latter require to be heated, the former may be used cold. To avoid the need of heating gelatin a solution is made and heated for several hours with the addition of a little ammonia; this when cool does not become solid, but after injecting (a dye being added) the preparation may be put into strong alcohol or dilute chromic acid and the mass sets.

*Cold Injection Fluids.*

Richardson's blue:

| | | |
|---|---|---|
| Solution No. 1. | Sulphate of iron, | 0.62 |
| | Distilled water, | 30.0 |
| Solution No. 2. | Red potassium ferrocyanide, | 2.0 |
| | Distilled water, | 30.0 |
| Solution No. 3. | Distilled water, | 60.0 |
| | Glycerin, | 30.0 |
| | Alcohol, | 30.0 |

Slowly mix 1 and 2, shaking; to the greenish blue opalescent fluid add 3 gradually, shaking.

Beale's Prussian blue:

| | |
|---|---|
| Glycerin, | 32.0 |
| Alcohol, 50 per cent., | 32.0 |
| Potassium ferrocyanide, | 0.75 |
| Tincture of perchloride of iron, | 4.0 |
| Distilled water, | 128.0 |

To one-quarter of the water and glycerin add the ferrocyanide, to another add the perchloride, add *the former to the latter* very gradually and shake in a bottle; add the alcohol and the rest of the water slowly with constant shaking. Preserve specimens in glycerin with 1 per cent. acetic acid.

*Warm Injection Fluids.*

Robin's gelatin vehicle:

| | |
|---|---|
| Gelatin, | 1 part. |
| Cold water, | 7-10 parts. |

Soak for a while, then heat over a water-bath; add 2 per cent. chloral hydrate to prevent mold; add for use one of the dyes given below.

Robin's glycerin-gelatin vehicle:

| | |
|---|---|
| Gelatin, | 50.0 |
| Water, | 300.0 |

(in which a little arsenious acid has been dissolved)

| | |
|---|---|
| Glycerin, | 150.0 |
| Carbolic acid, | 0.50 |

Mix on a water-bath in the order given.

Beale's carmin mass:

No. 1:

| | |
|---|---|
| Carmin, | 32.0 |

Moisten with a little water and complete solution by adding

| | |
|---|---|
| Ammonia, | 0.35 |

add, shaking

| | |
|---|---|
| Glycerin, | 15.0 |

No. 2:

| | |
|---|---|
| Glacial acetic acid, | 0.50 |
| Glycerin, | 15.0 |

Add 2 to 1 shaking and dilute for use with

| | |
|---|---|
| Glycerin, | 15.0 |
| Alcohol, | 7.5 |
| Distilled water, | 22.5 |

One part of this mixture is added to 3-4 of either vehicle given above. Such injection fluid is used warm and the object to be injected is kept in a large vessel of warm water till the operation is complete.

Prussian blue.

No. 1:

| | |
|---|---|
| Potassium ferrocyanide, sat. sol., | 90.0 |
| Glycerin, | 50.0 |

No. 2:

| | |
|---|---|
| Liquid perchloride of iron at 30°, | 3.0 |
| Glycerin, | 50.0 |

Mix slowly, combine with 3 parts of vehicle, add a few drops of hydrochloric acid.

**C. Imbedding and Sectioning.**—Two methods are employed for imbedding pathological material, namely with paraffin and with celloidin, the latter being somewhat easier to manage than the former. Each has for its purpose such impregnation of the tissue spaces with an indifferent and easily sectioned substance that the microtome knife will make thin and even sections without tearing and the various elements will retain their relations. Paraffin is a good example of an imbedding mass which is used hot and becomes firm on cooling. Celloidin works on the principle of solution in a volatile fluid, with firm consistency after the same has evaporated, and as a general rule the latter is used for large objects and the paraffin for small. Paraffin is best where very fine work is done and thin sections necessary, and yet, as it is brittle, material over 1.5 cm. on the edge may not give a thin section or perhaps even a complete one; and hence the method chosen depends on experience and convenience and the size and nature of the tissue to be cut. Where it is desirable to use paraffin for large pieces of tissue, a paraffin with a low melting-point ("soft" paraffin) will serve.

**Paraffin.**—Tissue must be well freed from water by absolute alcohol; dehydration may be hastened by laying material in anilin oil a few hours (up to 10). Then in

Xylol, changing two or three times, for about three hours at the outside, to remove the alcohol. Next in

Xylol and paraffin (see below) for 2-3 hours, and the process may be hastened by heating on a water-bath or a paraffin stove to about 52° C. Then in —

Melted paraffin. Two grades of paraffin are all that are usually needed in laboratory work, one melting about 56° C. and the other about 45° C. By combining these in different proportions a mass may be obtained which will be suited to the temper-

ature of the laboratory, using more hard for warm weather and more of the soft for cold. Thus 25 gm. hard with 30 gm. soft will give a mass whose melting-point is about 52° C., and will serve quite well for ordinary room temperature (up to 20° C.). By using a hot or cold knife according to circumstances the same mixture will cut over a wide range of temperatures. The paraffin is melted in a water-bath or a special oven at a constant temperature. Sometimes it cuts better after strongly overheating, which is equivalent to raising its melting-point, for the next time it requires more heat. A little of the melted paraffin is poured into a glass dish, which may be lightly wiped with clove oil or glycerin beforehand to prevent sticking. When nearly solid, the tissue is set in and more paraffin poured till the material is covered; the whole is then rapidly cooled by setting the dish a little way into cold water, or on a marble slab. Rapid cooling prevents crystallization and brittleness. Water must not touch the paraffin at any time during the process. Instead of glass dishes little cases and cylinders may be made of stiff paper, wrapped about blocks of wood, or a cork may be put into a short glass tube, paraffin poured on this, the tissue added, and the plug of paraffin and specimen thus formed pushed out when hard. The superfluous mass is pared off before cutting, paper removed, fastened to a block of hard wood or hard paraffin by the aid of heat, clamped in the microtome and cut, with the knife at right angles if the block is small, and somewhat slanted if larger. The former is apt to give a section smaller than the surface of the tissue, from squeezing and compression; the latter is apt to give a rolled or curved section. This may be controlled by lightly holding the section by a camel's hair brush as it is cut, or as in serial cutting. The steps of ordinary imbedding are then as follows:

1. Alcohol, absolute, to dehydrate (perhaps with anilin oil), 8 to 12 hours.
2. "Clearing," or impregnation with xylol, change 2 to 3 times, 2 to 3 hours.

3. Xylol and paraffin 2 to 3 hours.
4. Paraffin, melted; change once or twice; 2 to 5 hours.
5. Pour in mold and harden quickly.
6. Trim and fasten on block for cutting.

Rapid method for diagnosis of tissue scrapings, etc.

Tissue small and 1 to 3 mm. thin on blotting paper or cotton in absolute alcohol, ½ to 1 hour, change once.

Then in closed glass vessel with anilin oil, and put in thermostat or paraffin stove at 50 to 55° C., ½ to 1 hour.

Xylol changed 2 to 3 times, ½ to 1 hour.

Paraffin, melted, once changed, ½ to 1 hour.

Mold, pare and cut.

Several other fluids besides xylol can be used, as:

Turpentine, which may injure delicate tissues.

Clove oil, penetrates well, mixes with paraffin badly.

Chloroform, mixes well, requires to be driven off completely by heat, penetrates slowly, hence reserved for small objects and those hardened in chromic and osmic acids.

Bergamot oil, good for delicate tissue and to prevent shrivelling, used in equal parts with alcohol for 2 hours, then pure, then the soft paraffin, and lastly the mixture given above.

Anilin oil, used occasionally, good dehydrating agent.

Cedar wood oil, one of the best, penetrating well, not making tissues brittle as clove oil does.

**Sectioning.**—Paraffin preparations are cut dry, no alcohol or other fluid being used on the knife, and the blade is usually at right angles (to the long axis of a sliding microtome). If of the right consistence the sections are even and uniform and do not roll. For further handling they may be fastened to a slide or a cover-glass by either of these two methods:

Float the sections on water at 45° C. in a rather large and

shallow vessel. They smooth themselves out and may be picked up by sliding a perfectly clean glass slip under them, tilting to let the water flow away, or lightly touching with bibulous paper or pressing with the finger tip, then laid in the thermostat at 37° C. for 2 to 3 hours; or more rapidly, dried on the slide by holding it over a flame till the paraffin *begins* to look transparent. Or

Egg albumin is whipped and filtered, equal quantities of glycerin added, a slide very thinly coated and then heated to about 70° C.; cool, float a film of distilled water on the slide, lay the section on this, warm slightly if wrinkled, dry off water by filter paper, lay in thermostat 3 to 4 hours.

Before staining the section the paraffin may be removed by 5 to 10 minutes treatment with chloroform, xylol or turpentine oil, then in absolute alcohol 10 minutes; any desired method of staining may then be employed. Often the staining is quite as effective if the paraffin be not removed. Extra thin sections may be cut if a very little thin celloidin be brushed over the face of the block before each section is cut, but great care is needed not to use too much or to put it on the vertical side of the block. Each section as cut is laid on a slide with albumin fixative, celloidin surface down; meanwhile the coating on the next is hardening.

**Serial Sections.**—With a square set knife and a paraffin at about 45° C. melting-point, in a room temperature about 17° C., the edges of the block being pared away as much as possible and the front and back edges straight and parallel, with a very rapid stroke a series of sections may be cut, each of which clings lightly to the one just before and the one just after it, so that a ribbon is formed. Large divisions of this, containing many sections, may be picked up and handled at once, stained and mounted, making it possible to study the entire thickness of the tissue as section after section is passed in review. It is well to receive the ribbon as it is cut upon pieces of toilet paper, and if perfect they may be mounted at once. If they

show wrinkles or tend to roll they must be expanded, as also when the section is smaller than the cut surface of the block. For this purpose they are floated in groups on the surface of warm water or alcohol, or a number of them placed on a water film on a slide and heated, the water absorbed by blotting paper and the sections fixed in the thermostat or over a flame.

When fixed on the slide the paraffin may be removed by either benzol, chloroform, toluol or xylol. Various mixtures of these may be used, as also hot alcohol, creosote, turpentine and clove oil. The slide may be warmed till the paraffin begins to melt and at once plunged into a tube of xylol and mounted from it, or the xylol may be removed by alcohol and the sections stained.

Recapitulation of paraffin for small objects:

1. Enough cedar oil in a test-tube to cover the tissue.
2. Pour on the same amount of absolute alcohol.
3. Put the dehydrated tissue into the alcohol and wait till it sinks to the bottom of the oil; when the wavy lines at the junction of the two fluids have vanished, put the tissue into
4. Low melting-point paraffin; change once or twice.
5. Float the vessel on cold water when the tissue is filled with paraffin; when hard, cut a block containing the tissue and
6. Mount on a cone of harder paraffin already on the object-carrier of the microtome.
7. Cut serial sections, if desired, with thin celloidin if necessary.
8. Flatten the sections on warm water.
9. Float them on a slide.
10. Remove paraffin, stain, mount.

**Celloidin Method.**—Two grades of celloidin solution in equal parts of ether and alcohol are used, one of about the consistency of ordinary mucilage and the other as thick as molasses. The tissue is well dehydrated in absolute alcohol,

laid in equal parts ether and alcohol till quite saturated (1 to 3 days), then put in the thin solution for 24 hours, and an equal time in thick, but if there is no haste a longer time in each celloidin will be advantageous. For sectioning, the well impregnated tissue is mounted on blocks of glass or wood (cork is too yielding), and for wood the plugs used by ship-builders to conceal the nails in decks, hence called "deck-plugs," will be found useful. A film of celloidin is placed on the plug; before it is quite dry the tissue is placed upon it and allowed to become firm, which takes but a few minutes, a little more celloidin is poured on and about the tissue, building it up, and when the surface is fairly hard the whole is laid in chloroform or 80 per cent. alcohol till hard enough to cut. If the hardening on the plug is conducted slowly under a belljar to prevent too rapid evaporation of the ether, the result is better. Or a number of bits of tissue may be laid on the bottom of a shallow glass vessel, celloidin poured over them, the vessel covered loosely, and the cake formed in 12 to 24 hours cut and mounted as desired.

In cutting, the block of wood and tissue is clamped in the object holder of the microtome and the blade is set as slanting as possible consistent with sweeping the entire surface of the object; 80 to 90 per cent. alcohol is used to keep the blade as wet as possible, a thick camel's hair brush being convenient for the purpose and also to lift the sections as they are cut into a vessel of water, where they flatten out, or into alcohol. After staining the section, if clove oil is used to clear, it dissolves the celloidin, which allows delicate tissues and thin sections to fall apart. Oil of origanum (cretan, *not gallic*) oil of bergamot, oil of cedar, or xylol with carbolic acid do not dissolve the celloidin. The latter is made thus:

| | |
|---|---|
| Xylol, | 3.0 |
| Ac. carbolic cryst., | 1.0 |

For dehydration of sections a mixture as follows may be used:

| | |
|---|---|
| Chloroform, | 1 part. |
| Absolute alcohol, | 2 parts. |

If necessary to remove the celloidin, as often after the use of anilin stains which stain also the celloidin, put a few drops of clove oil on the section on a slide, after five to ten minutes remove the oil with a pad of bibulous paper and pour a few drops of xylol on the section: balsam, cover-glass.

Recapitulation of celloidin method:

1. Dehydrate with absolute alcohol.
2. Ether and alcohol, equal parts, 1 to 3 days.
3. Thin celloidin 1 to 5 days.
4. Thick celloidin 1 to 5 days.
5. Fasten on wooden plugs and dry 15-20 min.
6. Chloroform 2 to 5 hours; vapor of chloroform 12 hours or 80 per cent. alcohol 12 hours.
7. Cut wet with slanted knife.
8. Stain, clear with oil of origanum, etc.
9. Mount in balsam.

Keep the balance of the tissue on the plug in 80 per cent. alcohol, or pry the imbedded mass off the block and keep that in alcohol, labelled properly.

Combinations of paraffin and celloidin have been recommended but either method alone is satisfactory as soon as the details are familiar, if a little care is used; for pathological purposes the combined method is hardly necessary. It is as follows:

Imbed in celloidin.

Soak the imbedded material in oil of origanum (cretan) 12 hours or more till quite transparent.

Concentrated solution of paraffin in origanum oil 12 hours, heating to 40° C.

Melted paraffin at 50 to 52° C., 12 to 24 hours.

Harden, pare and mount on firmer paraffin, cut, etc.

**Glycerin-jelly Method.**—This method is rapid but does not permit very thin sections. The hardened tissue is left 24 hours

in thin mucilage (made with gum arabic) and glycerin, equal parts; then laid on a block, put in alcohol when firm, cut and stained; water, especially if slightly warmed, removes the imbedding mass.

**D. Staining Methods.**—The principle upon which the technique of staining depends is that certain cells and parts of cells display a special affinity for certain dyes, thus becoming prominent in the section and permitting closer study. It must never be forgotten that a stained tissue is not strictly a normal picture, and hence it is well as a matter of routine to examine unstained preparations both before and after other similar sections are stained, in order to correct and supplement the details brought out by the dyes. Certain anilin and other colors stain nuclei especially well, others color the cell body or the interstitial substance. By combining two or more we obtain polychromatic pictures of the greatest value. If a single stain colors different tissue elements different colors in one staining it is called metachromatic, as gentian violet and methyl violet, which stain amyloid material red and the rest of the tissue blue-violet. From a chemical standpoint the stains are divided into basic, neutral and acid; in the first the staining element acts as a base, combining with acid cell constituents (nucleo-phosphoric acid?) like fuchsin and magenta; the acid stain is one where the coloring agent acts as an acid, like acid fuchsin; neutral stains are usually made by artificial combinations of acid and basic stains. In a general way the basic stains are nuclear or chromatin stains, and the acid are cell or plasma stains. Both usually require differentiation after their use, that is, if a nuclear stain has been employed the cell body is lightly and diffusely colored while the nucleus is deeply stained and the color must be removed from the plasma in order to make the nuclei clearer. (See p. 368.) As decolorizers we may use distilled water, alcohol, anilin oil, weak acid in water or alcohol, and weak alkaline solutions.

General rules:

1. Good staining requires the tissue to be properly fixed and hardened; fresh material and tissue left too long in alcohol or chromic acid and its mixtures may not stain at all.
2. Staining materials must be of the best, obtained from some reliable firm, carefully prepared, and always filtered before use to avoid precipitates in the tissue.
3. Sections should be properly spread out in relatively large quantities of the stain and should not lie upon each other, to prevent the fluid reaching their surfaces unequally.
4. As to the rapidity of staining solutions and combinations, only the indefinite statement may be made that old and ripened stains usually are quicker than those freshly made; but the previous treatment of the tissue is also of importance.
5. The staining power may be increased by
   (*a*) Strengthening the concentration of the dye.
   (*b*) Heating to 30 to 40° C.
   (*c*) Adding mordants, like acids and alkalis, alum, anilin oil, etc.
6. Decolorizing agents must be entirely washed out after use or the stain rapidly bleaches in the mounted preparation.

## Nuclear Stains.

**Carmin.**—This gives good and lasting stains but the solutions are liable to spoil after keeping a short time.

1. *Alum Carmin.*

| | |
|---|---|
| Carmin, | 1 |
| 5 per cent. alum solution, | 100 |

Boil 20 minutes, cool, filter; good for tissue hardened in alcohol, sublimate, Müller's fluid, and formalin.

Sections from distilled water:

(*a*) In the stain 10 min. to several hours; overstaining does not occur;

(*b*) Washed several times in distilled water;

(*c*) Mounted in glycerin or carried through alcohol, oil and balsam.

Nuclei are red with a bluish tinge, cell body pale.

2. *Lithium Carmin.*

| | |
|---|---|
| Carmin, | 2.5 |
| Sat. sol. lithium carbonate, | 100 |

Combine, with a mild degree of heat if necessary, cool, filter; good for tissue hardened as above.

Sections from distilled water:

(*a*) In the stain 5-10 min.; paraffin sections a little longer.

(*b*) Well washed.

(*c*) Differentiated in alcohol (70 per cent.) 100 parts, hydrochloric acid 1 part, 5-10 min.

(*d*) Wash thoroughly.

(*e*) Mount in glycerin or alcohol, oil, balsam.

Nuclei deep red, the other tissue elements pink or colorless according to the differentiation. This stain may cause the tissue to swell badly because of the large per cent. of alkali; paraffin sections should be fastened to the slide first.

3. *Borax Carmin.*

| | |
|---|---|
| Carmin, | 0.5 |
| Borax, | 2.0 |
| Distilled water, | 100.0 |

Mix, boil, stir constantly with a glass rod and add drops of 0.5 per cent. acetic acid till deep red color is obtained; let stand 24 hours, filter.

Tissue hardened as above.

Sections from distilled water:

(*a*) In stains 5 to 20 minutes.

(*b*) Washed.

(*c*) Differentiated in hydrochloric acid and alcohol as above.

(*d*) Thorough washing.

(*e*) Alcohol, oil, balsam.

Nuclei are red.

Hematoxylin.—This is one of the best and most generally used of the non-anilin stains; good for usual hardenings, except after chromic and osmic acids and mixtures, but Delafield's hematoxylin gives good results with long staining. None of the hematoxylin mixtures is active when first made, having to go through a ripening process of several days to weeks. As this is essentially an oxidation by which hematein is formed, the addition of hydrogen peroxide to the fresh stain accomplishes the same result without loss of time. The strength, that is, staining power, increases with age, hence a moment or two will be long enough with an old solution and 15 to 20 minutes may be needed for a recent one. Filter the stain each time before use; afterward return it to the bottle through a filter, as it may used again indefinitely. Sections when once stained may be washed in water from 30 minutes to several hours, and if there is a little alkali present (less than 0.5 per cent.) the differentiation is more complete. Nuclei are deep blue, plasma bluish, according to the differentiation; mucus, lime salts and cartilage are also stained. Excess stain may be removed by the following, and sometimes it is well to overstain on purpose and control the decolorization till the desired color is reached:

Hydrochloric acid alcohol as given above, well washed out

with ordinary water; usually 30 seconds to 3 minutes is long enough to clear up any but the deepest overstaining. The color turns reddish brown in the acid, becomes blue again in water. A few drops of saturated lithium carbonate solution hasten the removal of the acid.

Alum in 0.5 per cent. solution is slower than the acid alcohol, but for that reason it is easier to obtain any desired depth of stain.

The following are the commoner hematoxylin solutions used in pathology:

1. *Böhmer's.*

| | | |
|---|---|---|
| A. | Hematoxylin (cryst.), | 1 gm. |
| | Absolute alcohol, | 10 cc. |
| B. | Alum, | 20 gm. |
| | Hot distilled water, | 1000 cc. |

Filter while hot.

After standing 24 hours the two solutions are mixed and ripened for a week in open wide-mouthed bottles.

2. *Delafield's.*

| | |
|---|---|
| Hematoxylin (cryst.), | 4 gm. |
| Absolute alcohol, | 25 cc. |

Dissolve and add to

| | |
|---|---|
| Saturated ammonium alum sol., | 400 cc. |

Ripen 5 to 7 days in unclosed bottle, frequently stirring with glass rod, then add

| | |
|---|---|
| Methyl alcohol, 95 per cent., | 100 cc. |

and preserve in well-stoppered bottles. For use, take equal parts of stain and distilled water.

3. *Friedländer's.*

| | |
|---|---|
| Hematoxylin (cryst.), | 2.0 |
| Absolute alcohol, | 100.0 |
| Distilled water, | 100.0 |
| Alum, | 2.0 |
| Glycerin, | 100.0 |

4. *Ehrlich's acid hematoxylin.*

| | | |
|---|---|---|
| A. | Hematoxylin, | 2.0 |
| | Absolute alcohol, | 60.0 |
| B. | Glycerin, | 60.0 |
| | Water, | 60.0 |
| | Alum to saturation, | |
| | Glacial acetic acid, | 3.0 |

Mix, ripen in open vessel a week, keep in well-stoppered bottles and precipitates seldom form, overstaining even with old solution not common.

Sections from distilled water:

(*a*) In stain 3 to 10 minutes, less with old stain.
(*b*) Washed 30 minutes to several hours.
(*c*) If overstained, use acid alcohol or alum solution.
(*d*) Wash out well.
(*e*) Mount as desired.

5. *Mayer's' hematein.*

| | | |
|---|---|---|
| A. | Hematein, | 1.0 |
| | Alcohol, 90 per cent., | 50.0 |

Dissolve with heat.

| | | |
|---|---|---|
| B. | Alum, | 50.0 |
| | Distilled water, | 1000.0 |

Mix A and B, cool, filter. Gives very deep stain at once, does not require ripening; with the addition of glacial acetic acid (2 per cent. of the entire mixture), very satisfactory results are obtained.

## Anilin Stains.

Tissues which have been hardened in chromic acid or its salts may not take the stain, otherwise the action is quick and simple. Many of these do not last very long, the tissue bleaching out even when kept in the dark, and glycerin mounts are

the least durable. Solutions seldom remain active for longer than a few weeks and should be filtered before use. Bacteria grow freely in some solutions and should be controlled by the addition of a few drops of carbolic acid.

1. Bismarck brown or Vesuvin:

| | |
|---|---|
| Vesuvin, | 2.0 |
| Alcohol (90 per cent.), | 60.0 |
| Distilled water, | 40.0 |

Heat to boiling, cool, filter, add 5 per cent. carbolic acid solution, 10 drops.

Sections from alcohol:

(*a*) In stain 5-10 min.

(*b*) Washed in alcohol.

(*c*) Mount in balsam after clearing; or in glycerin, which does not destroy this stain.

Nuclei brown, plasma lighter, mucus and bacteria stain also.

2. Gentian violet:

| | |
|---|---|
| Gentian violet, | 2.0 |
| Distilled water, | 100.0 |

Heat, cool, filter. Methyl blue is prepared in the same way. For other combinations see pp. 302-3.

Overstaining, especially with gentian violet, very apt to happen but may be corrected with plain or acid alcohol. Mount in balsam.

3. *Fuchsin.*

| | |
|---|---|
| Fuchsin, | 1.0 |
| Alcohol (40 per cent.), | 100.0 |

Heat, cool, filter. Use as for vesuvin. The addition of 2 per cent. acetic acid gives a good stain for fresh material, not hardened, and may be carried under the cover-glass by blotting paper.

4. *Safranin.*

| | |
|---|---|
| Safranin, | 1.0 |
| Alcohol (30 per cent.), | 100.0 |
| Distilled water, | 200.0 |

Heat, cool, filter; dilute one half for use.

Sections from alcohol.

(*a*) In stain up to 24 hours.

(*b*) Washed in water.

(*c*) Washed in acid alcohol—HCl 6-8 drops, or sat. picric acid in water, 10 drops; alcohol, 100 cc.

(*d*) Washed in absolute alcohol till no more clouds of stain are withdrawn.

(*e*) Cleared in oil or xylol, mounted in balsam.

Resting nuclei are pink, mitotic figures deep red, mucus yellowish-red, fibrin (after Flemming's hardening fluid) deep red.

For more rapid results:

| | |
|---|---|
| Safranin in excess, | |
| Distilled water, | 100.0 |
| Anilin oil, | 2.0 |

Heat to 70° C., filter through wet paper. The stain is almost instantaneous, used as above.

## Diffuse and Double Staining.

Diffuse staining occurs in pathological technique as contrast stain for all tissue elements except nuclei, the latter being of a deep and different color and hence more prominent on the diffuse background. Blue and violet nuclear stains are used with a reddish plasma stain, red nuclei are displayed on a yellow background. The nuclei are usually stained first in stronger fluid and then the weaker contrast is used.

1. *Ammonia Carmin.*

| | |
|---|---|
| Carmin finely powdered, | part. |
| Aq. ammon. fort., | 1 part. |
| Distilled water, | 75 parts. |

Mix, allow the ammonia to evaporate, filter, ripen several weeks before use. Keep tightly corked as the solution becomes rapidly moldy. This stain may be prepared by rubbing the carmin and ammonia together in a large glass mortar, spreading the thick mass over the whole inner side to dry, then repulverized, allowed to stand 24 hours in an open vessel, and dissolved for use in cold distilled water; this is ready immediately, requiring no ripening. Staining power increases with age.

To use, add the stock solution by drops to distilled water till pale red; in this put sections from distilled water for 12--24 hours; wash, dehydrate, clear and mount. Stronger solutions are quick but indistinct in results. Sections are best stained if laid flat on bibulous paper, not allowed to cover one another. Heating to 40-50° C. is necessary for tissues hardened chromically.

Nuclei, plasma, fibrous tissue, muscle fibers of both kinds, decalcified bone, neuroglia, axis cylinders and hyaline material will be stained; elastic tissue, basement substance of hyaline cartilage, nerve sheaths, mucus, fat, and corneous epithelia are unstained. Hematoxylin stain first is to be recommended.

**Picric Acid.**—A few drops of saturated alcoholic or aqueous solution added to distilled water, sections treated for a short time (up to 5 min.) washed in water or alcohol, if too much stained decolorized in 1 part saturated solution lithium carbonate to 10 distilled water. Plasma, red cells, muscle cells, fibrous tissue, fibrin, hyalin, corneous epithelia are stained yellow.

Picric acid is seldom used alone. With hematoxylin and safranin it partly removes the first stain, hence overstain before putting sections into the picric acid. Among the combinations of this kind picro-lithium carmin is one of the best:

| | |
|---|---|
| Lithium carmin solution, | 1 to 1½ parts. |
| Picric acid, watery solution, | 2 parts. |

Or Friedländer's mixture may be used:

| | |
|---|---|
| Carmin, | 1 part. |
| Liq. ammon. fort., | 1 part. |
| Distilled water, | 50 parts. |

Stir and add, a drop at a time, saturated watery picric acid solution, 1-4 parts according to the percentage of ammonia present: filter and add 10 drops carbolic acid. Stain 5-10 min., wash, decolorize with acid alcohol 2-5 min., wash in distilled water 10 min., alcohol, oil, balsam.

**Eosin.**—There are two kinds of eosin, one soluble in water and the other in alcohol. The use of either is largely a matter of choice. It is the commonest contrast stain after hematoxylin, used in 0.1 to 1.0 per cent.; acts very quickly but the excess easily comes out in alcohol. Tissue may be fixed in formalin or sublimate, stained in hematoxylin, decolorized in acid alcohol, washed in several waters, stained in 1 per cent. eosin in alcohol, again washed in water and allowed to lie in water or alcohol till no more red is apparent to the naked eye, dehydrated and mounted in balsam. The erythrocytes are brilliant red and the tissue resembles a fine injection as the vessels are everywhere prominent; eosinophile cells are easily found. The eosin can be put in the clove or origanum oil used for clearing, but better results are obtained as above.

Biondi-Heidenhain method:

| | |
|---|---|
| Methyl green, saturated aqueous solution, | 50.5 |
| Orange, saturated aqueous solution, | 100.0 |
| Acid fuchsin, saturated aqueous solution, | 20.0 |

The separate solutions stand for a few days with excess of dye before mixing; for use one part is diluted with 100 parts

distilled water. A drop of this on a filter paper makes a spot which is bluish-green in the middle, orange on the circumference, if there is a zone of red external to this too much fuchsin is present. Harden in sublimate, imbed in paraffin; if the tissue has lain long in alcohol, wash it in 0.1 per cent. of acetic acid 1 to 2 hours, then in water.

Sections from distilled water in stain 24 hours, 90 per cent. alcohol 1 to 2 minutes, dehydrate rapidly in absolute alcohol, xylol, balsam.

Resting nuclei are bluish-green, dividing nuclei and fragmented leucocytes are deeper blue-green, plasma and fibrous tissue are red, erythrocytes are orange-red, fibrin red, mucus green. Method unreliable, and color soon lost from nuclei.

Van Gieson's method.

Tissue hardened in alcohol, formalin, sublimate, Müller's fluid; cut, overstained in Delafield's hematoxylin, well washed; then 3 to 5 minutes in:

| | |
|---|---|
| Saturated aqueous picric acid, | 150 cc. |
| Acid fuchsin solution, | 3 cc. |

Wash in water half a minute, dehydrate, oil, balsam. Nuclei deep brownish-red, fibrous tissue and hyalin (of epithelial origin) red, muscle cells red, remaining tissue yellow.

## E. Bacteriological Methods.

**Sterilization.**—Every utensil, test-tube, knife and culture-vessel must be free of bacteria, or the results obtained cannot be trusted. To obtain this required cleanliness two methods of sterilization are employed: by heat and by chemical solutions. Heat is applied as dry or as moist heat. The former requires that objects to be sterilized be kept at a temperature above 100° C. for a relatively long time, and as the power of penetration of dry heat is limited, the method is reserved for glass plates, knives, small dishes and other utensils which are not injured by the high temperature. The articles to be sterilized are placed

in a hot-air oven of Swedish iron, double-walled, with a double door and a bottom of heavy copper, and kept for at least an hour at 100° to 150° C., or even 180° C. Under this heat, supplied by Bunsen burners, the copper plates which form the bottom are apt to be burnt out in time. The oven should be well jacketed with thick asbestos to lessen the radiation.

Moist heat is more commonly used for sterilization, usually as flowing steam; its power of penetration is greater, and it may be used at a lower temperature than dry heat with less damage to the articles in the oven. By an arrangement which supplies the steam under extra pressure, the penetration and degree of heat increase with good results where clothes and other fabrics require to be treated. In the laboratory the various fluids and solids used as culture media would be ruined if sterilized at the high temperature of the dry method, and many spores resist the dry, while they succumb readily to the moist heat.

The application of the heat varies with the method. Dry heat is always continuously applied till the objects are sterilized. With steam the fractional method is more often used. The principle is that a short exposure of a culture medium to flowing steam will destroy all the mature bacteria which may be present, but perhaps not the spores. The latter are given time to develop at ordinary room temperature, and the medium is for the second time exposed to steam and any bacteria which may have developed in the interim are destroyed; a second repetition is usually required, and in some cases even more. The media would be rendered sterile if exposed for hours at the same temperature, and the spores either would not develop or would die in the process, but the medium, being composed of organic materials, such as gelatin, milk, broth, etc., would be rendered unfit for the future growth of bacteria in them, hence the value of the fractional method. The custom is therefore to expose the media to steam, in test-tubes and other containers, for fifteen to twenty minutes, on three succeeding days, at about the same hour.

Fractional sterilization at a low temperature is carried out in the same way, but the temperature is regulated at about 65-70° C., and this method is used where the substance to be treated will not endure a high degree of heat, as in the case of blood serum; an hour's exposure being given for three days and the material kept at about 30° C. between times.

A third way of using steam, under pressure of at least one additional atmosphere, which is equivalent to raising the temperature to 122° C., and which will usually destroy all bacteria and their spores in less than half an hour, is sometimes employed in the laboratory, more often in disinfection for hygienic purposes. It is difficult to control the time of the exposure by this method, for when the required degree has been reached it will not do to open the autoclave, since the sudden relief of pressure causes the fluids to escape from their containers. Articles must thus be exposed while the temperature is rising, for the required time at the proper degree, and also while the oven cools enough to permit opening it.

As used in the laboratory the forms of steam sterilizer resemble the original oven designed by Koch, and consist of a metal cylinder, the lower part containing a reservoir for water and a protected space for the application of heat, the upper and larger portion being double-walled or jacketed with felt for the prevention of radiation, and communicating freely with the water chamber for the reception of the steam. Objects are placed in the upper part, tightly covered, heat applied below, and steam allowed to flow through the apparatus for the desired time. The water chamber has a gauge to show the amount of water present, and unless the supply is copious the bottom may burn out. An Arnold steam sterilizer may also be employed for ordinary work.

When the sterilizer has a tight-fitting cover, which may be screwed down so that no steam can escape, and a safety valve on top for control, it is called an autoclave, and works on the principle of steam under pressure, as above.

Knives, forceps, slides and platinum loops may be sterilized by holding them for a short time in the flame of a Bunsen burner.

Chemical sterilization is seldom used except for utensils, as the chemicals would injure media and prevent the growth of bacteria. The commonest solutions used for chemical sterilization, with their strengths, may be seen by referring to Table of Antiseptic Solutions, p. 314.

These fluids act by forming chemical combinations of unknown constitution with the substance of the bacteria, but even corrosive sublimate, one of the strongest, may not kill the bacteria, for if the mercury salt is removed within a short time the germs may be able to go on living.

**Culture Media.**—These may be either natural or artificial, fluid or solid:

| | *Natural Media.* | *Artificial Media.* |
|---|---|---|
| **Fluid** | Blood serum,<br>Hydrocele and ascitic fluid,<br>Urine,<br>Eggs, uncooked,<br>Milk. | Mixed chemical solutions,<br>Beef and other broths,<br>Vegetable infusions. |

| | *Natural Media.* | *Artificial Media.* |
|---|---|---|
| **Solid** | Blood serum, coagulated,<br>Potatoes,<br>Eggs, cooked,<br>Sterilized organs. | Broth or<br>Milk with a solidifying substance added, as<br>Gelatin or agar. |

1. **Natural Media.** *Blood Serum, Fluid.*—Blood is drawn from a healthy animal at the time of slaughtering by incising a vessel and allowing the blood to pass into a sterile jar. The latter is covered and put in a cool place and the clot allowed to form, a sterile glass rod gently detaching it from the side if necessary. When coagulation is complete the clear serum may be siphoned off into sterile test-tubes or other containers. If

everything has been sterile the serum is safe to use, either fluid or solid, without sterilization.

2. *Blood Serum, Solid.*—Siphon off the serum into sterile test-tubes, a few cc. in each, lay these in a hot-air sterilizer, slanted, and raise the temperature to 80° C., not higher; the serum sets and is clear straw color, opalescent; the tubes are then sterilized at 90° C. in steam thirty minutes a day, three days.

Löffler's serum mixture:

| | |
|---|---|
| Broth with 1 per cent. glucose, | 1 part. |
| Serum, | 3 parts. |

Mix, fill tubes, raise to 65° C. an hour a day for three days, or sterilize as above; good for many kinds of bacteria, especially diphtheria.

3. *Eggs* may be sterilized by the low temperature method and a small hole made in one end by a sterile instrument, inoculated through the opening and closed with wax or paraffin; if dipped in paraffin there is less evaporation of contents.

4. *Milk,* deprived of its cream by standing in a cylindrical vessel and then drawn off by a stopcock at the bottom, or "separator" milk from butter factories, sometimes is useful, as certain bacteria coagulate it or peptonize it; with a little litmus added the reaction of the growing bacteria is apparent. Test-tubes are charged with it and sterilized in steam three days; care and thoroughness especially necessary as milk when delivered is usually full of bacteria and their growth is rapid.

5. *Urine* may be occasionally used, as also hydrocele and pleuritic or ascitic fluid, but generally the ordinary media are quite sufficient.

6. *Potatoes* are of great value in routine laboratory work. They should be of medium size, free from bruises and spots. Scrub them well with a brush and ordinary water, then with 1 to 1,000 bichloride solution, rinse in sterile water and sterilize in steam for an hour for three days or in the autoclave half an hour. Cut across with a sterilized knife they may be inoculated

on the smooth surface and the bacteria developed in the thermostat, the potato lying in a sterile dish with a cover. Before sterilizing a series of semicylindrical pieces with one slanting side may be cut, these slipped into test-tubes with a few drops of water and sterilized in steam by either method. Other vegetables may be used, as carrots, but the potato is sufficient. It is well to soak the cut potato in several changes of water, or wash it with a weak alkaline solution, for its own reaction is often strongly acid.

7. *Various organs* of lower animals may be sterilized and used for streak cultures, and human skin, freshly obtained after death and treated with digestives (pepsin, pancreatin), is at times useful. Cat kidneys halved and sterilized will serve for some difficult bacteria (streptothrix).

1. *Dunham's peptone solution.*

| | |
|---|---|
| Pure peptone, | 10 gm. |
| Sodium chloride, | 5 gm. |
| Distilled water, to make a paste. | |

Rub well in a mortar and afterward dilute to 1,000 cc., boil and filter, sterilize; it is ready for use and is employed to test for indol in growing cultures.

2. *Potato Extract.*—Rub 500 gm. potato with 500 cc. distilled water, decant, dilute to 1,000 cc., add 40 gm. glycerin; good for tubercle bacilli.

3. *Hay, malt and other vegetable infusions* have been used for particular purposes but find little applicatian in ordinary bacteriological work.

4. *Beef Broth; Bouillon.*—Of all fluid media this is the commonest and most useful. It is made by soaking lean beef, free from gristle or fat and chopped fine in a mincing machine, half a kilo (about one pound) in 1,000 cc. water 12 hours; squeeze the meat in a coarse towel and filter the total liquid obtained. Add sodium chloride 10 gm. and peptone 5 gm. Test for re-

action and slightly alkalize by sodium hydrate solution, 10 per cent., added in drops; litmus will do for the test but phenolphthalein is better, 1 gm. dissolved in 1,000 cc. 50 per cent. alcohol. To use, several watch glasses are arranged in series with 1 cc. of the solution in each; a drop of the broth is added to the first, more sodium solution is added to the broth and another drop tested; when alkaline the test solution turns rosy red. At this point salts and proteids insoluble in alkaline media precipitate and broth becomes cloudy; it may be necessary to boil and filter and alkalize again. For tubercle bacilli 6 per cent. glycerin may be added to this alkaline bouillon. Various bacteria cloud this medium or form a film on the surface or change the reaction or fall as a light cloud to the bottom. To use in a solid form, glycerin and agar are added to the broth.

5. *Beef Peptone Gelatin.*—To 1,000 cc. cool broth add in small pieces 100 gm. "gold leaf" gelatin (a higher per cent. is used in hot weather), soak twenty minutes or till well swollen, dissolve by gentle heat on a water-bath, remove and cool to 50° C., alkalize with great care. If too alkaline it will not set, correct by a few drops of 5 per cent. acetic acid, the reaction must be faintly alkaline. Now mix a broken egg, shell and all, into the medium and boil half an hour over a flame covered with wire gauze, adding water as it evaporates. The flask may simply be set in the steam sterilizer and boiled till clear. Try it by putting a little in a test-tube and repeatedly boiling, if still clear and right in reaction, filter the rest into test-tubes, sterilize, and properly cork with cotton. It is perfectly clear when well made and solid below 22° C. Certain bacteria produce a proteolytic ferment which liquefies this medium.

6. *Beef Peptone Agar.*—Small pieces of agar, 10 gm. in all, are added to 1,000 cc. cold bouillon, boiled an hour with frequent stirring, water added as required and the whole filtered. In filtering both gelatin and agar a jacketed filter is sometimes used, kept hot by a Bunsen burner, but this entails evaporation

and thickening of the medium and is not necessary if the solution is perfect and if a little is added at a time to the filter, the rest being kept hot on a water-bath. The fluid should be poured carefully along a glass rod onto the side of a properly folded filter paper. Gelatin must not be boiled too long or it will not set; agar may be boiled indefinitely but may stick to the vessel. Agar is not so clear as gelatin but it is solid below 42° C. and hence may be put in the thermostat at body temperature, which is optimum for many bacteria. Various mixtures may be employed, glycerin, neutralized urine, glucose, lactose, etc., for special purposes.

Instead of beef or veal for these media, Liebig's or Armour's extract of beef may be used.

**To Clean and Fill Test-tubes.**—Fasten a wad of cotton on the end of a strong glass rod, dip in nitric acid and swab the inside of the tube, rinse four times in water, drain, and, when nearly dry, rinse with 95 per cent. alcohol, dry, sterilize. Plug the tubes with cotton and sterilize in hot air at 150° C. till the cotton turns brownish. By a short rubber tube connect a filter and a short glass tube, a pinch-cock on the rubber part; insert the end of the glass tube part way down a test-tube and release the pinch-cock till 5-8 cc. broth or other medium are in the tube, shut off, re-apply the cotton plug, sterilize three times for half an hour in steam. The fluid must not touch the rim of the test-tube or the cork will stick. Other vessels, Erlenmeyer flasks, etc., may be treated in the same way. If the cotton plugs are covered with tin foil while in the sterilizer the steam does not condense upon them; covered with rubber caps they do not dry out on long keeping. Having prepared tubes with gelatin, agar and serum allow some of them to lie at a slant so that when set they will present a broad surface for inoculation; others are kept upright for stab cultures. If laid for 24 hours nearly horizontal at room temperature the gelatin and agar slants will not slide down in the tubes. If the tubes are wanted for anerobic cultures they must be half

filled with the medium that the bacteria may develop in the depth away from the air.

**Kinds of Cultures.**—The usual forms of cultures are:

1. Stab.
2. Slant.
3. Plate.
4. Petri dish.
5. Esmarch roll.
6. Hanging drop.
7. Anerobic.

(1) The first is made by holding a platinum wire, fused to one end of a glass rod, in the flame till it glows. With this sterile wire, which may be straight and slightly flattened or looped at the end, some of the material to be studied is picked up, the cotton plug of a sterile and charged tube is held between the fingers of the left hand while the tube itself is held by thumb and first finger, the loaded needle is sunk straight to the bottom of the solid gelatin or agar or stirred about in fluid media. The stab must be straight and in the mid axis of the tube and the needle should not be allowed to touch the side. The cork is replaced, the platinum wire is again heated in the flame. Before and after charging a tube thus the cotton plug is set on fire for a moment and the opening of the tube passed through the flame, to destroy chance germs. Such a tube is then incubated at room temperature if containing gelatin or in the thermostat at constant temperature if agar or serum or broth. When it contains but one kind of microörganism and its brood it is called a pure culture, otherwise it is a mixed or contaminated culture.

(2). Slant surfaces of solid media, agar, serum, potatoes, etc., are inoculated in a similar way by drawing the charged loop over them.

(3) For plate cultures small squares or oblongs of glass are sterilized in hot air. Three tubes of gelatin or agar are melted and kept in a water-bath; matter to be studied is introduced

into one, a platinum loop or two of this fluid medium with bacteria, is used to make a dilution in the second tube, a loop or two from the second inoculates the third; the needle flamed between each two. The tubes are marked in chalk or by labels with the date, kind of material, and a number for each. A sterile plate is laid on a larger piece of glass which in turn rests on the surface of cold water in a container, the melted inoculated medium of tube No. 1 is poured carefully on it and guided with a glass rod so that it sets with a margin of clear glass all about it — this film when solid again presumably contains many and probably different bacteria scattered singly over the plate, and where they are lodged each will develop into a colony. But as the first plate usually contains altogether too many colonies, dilution No. 2 makes plate No. 2 and dilution No. 3 makes plate No. 3, and one of these latter will contain so few colonies, when incubated, that different kinds may be recognized, lifted out bodily with the broad ended platinum wire, and used to make a pure culture in a new tube. When the three plates are poured and set they are piled one on the other, No. 1 lowest, each separated from the others by little glass bridges, and the whole in a sterile dish with a cover, and at the end of 12--24 hours in the proper temperature they are ready for examination.

(4) Such plates have been nearly given up in favor of similar cultures in the Petri dish, a shallow glass dish with a cover, which may be set on the stage of a microscope and examined without removing the cover and risking contamination by matter floating in the air.

(5) Another device is the rolled culture or Esmarch tube. A test-tube of melted medium is inoculated, laid on a block of ice with the stopped end but little higher than the other, and rotated, slowly at first then rapidly. The film sets all round the inside and bacteria develop where caught and the unopened tube may be examined by a magnifying glass or the low powers of the microscope.

(6) The hanging drop culture is made by using perfectly clean hollow-ground slides; a ring is made with vaselin round the depression in the slide; a cover-glass is sterilized and laid on a wire gauze under a belljar. In the middle of the cover-glass a drop of beef broth is placed, this is inoculated with any desired pure culture, the platinum needle being flamed and allowed to cool between placing the drop and inoculating it. Afterward the cover-glass is carefully reversed over the ring of vaselin, slightly pressed to shut out the air, and the preparation set away in a moist chamber at 37° C. to incubate; in 12-24 hours it may be studied with the higher powers. A small ring of hard rubber and an ordinary slide may be used instead of the hollow slide.

(7) An anerobic culture may be made by deeply inoculating a tube more than half full of solid medium, the germs developing in the deeper portion away from the air; or melted paraffin may be poured on the top of the medium, or oil, to shut out oxygen; or a stream of hydrogen may be passed into the tube and the glass tube by which it enters closed by a flame.

**Inoculation of Animals.**—Mice may be inoculated with any pure culture or suspected material by cutting a small pocket in the skin just over the root of the tail, after clipping the hair close, and depositing it within the pocket or farther from the wound along the back; special mouse holders are sold for the purpose. Or a hypodermic syringe carries the inoculated broth culture into the peritoneal cavity, after clipping and disinfecting the skin and sterilizing the needle. Rabbits, guinea-pigs, pigeons and other small animals may be used similarly, an assistant holding them quiet while a surface of skin is cleaned and the inoculation practiced. The rabbit is often inoculated through the posterior branch of the large vein of the ear, directly into the circulation. When solid pieces of tissue are introduced into the serous cavities of animals a careful surgical operation must be done, with complete asepsis, and the wound carefully closed and dressed. After inoculating an animal

note and record at regular periods its temperature, loss of weight, position in the cage, appetite, diarrhea, reaction at the site of inoculation, etc. After the death of the animal make the post-mortem immediately and if delay is unavoidable always note in the record the exact amount of time elapsed. Make the external inspection, weigh, fasten on a sterile board with tacks or small nails, wash the whole body with 1-1,000 bichloride and rinse this off with sterile water. Apply (while still hot) a broad bladed knife which has been heated red to the linea alba and transversely across it, open through the charred lines, the skin only, and reflect and tack it to the board. The track of all incisions must be charred superficially in this way before opening. In making cultures from an organ a scalpel is reddened in the flame, laid on the organ, again heated and used to cut through the char, a platinum loop passed deep into the organ through the cut and twisted to gather some of the uncontaminated cells and fluids, and this is inoculated into any desired medium; instead of the loop the spade end may be used. Cover-glass preparations should be made at the same time from blood and exudates. For further study the organs may be cut out with sterile scissors and dropped into 95 per cent. alcohol or 3-5 per cent. formalin, imbedded, cut and stained. A careful record of the autopsy as a whole and of the organs from which smears and cultures are made must be kept.

## Staining Bacteria.

A few of the basic anilin colors are employed for staining bacteria, especially methyl and gentian violet, methylen blue, fuchsin, and Bismarck brown. They are kept in stock solutions (saturated alcoholic) and enough is taken at a time to color a 50 cc. bottle of distilled water so that the neck is just transparent, or added to a watch glass of distilled water to the point when the fluid becomes too dark to see through; in such strengths these dyes will stain nearly all forms of bacteria; the

thin solutions are good for about two weeks. To such solutions certain mordants are added to increase the power of the staining agent, and alkalis, carbolic acid, anilin, and ammonium carbonate are the commonest.

1. Löffler's Methylen Blue:

| | |
|---|---|
| Concentrated alcoholic methylen blue, | 30.00 |
| 0.01 per cent. potassium hydrate solution, | 100.00 |

This stains quickly, 5-10 minutes, and is fairly durable; for organisms hard to stain the potassium may be raised to 1.0 per cent.

2. Anilin gentian violet:

| | |
|---|---|
| Anilin oil, | 10 parts. |
| Distilled water, | 100 parts. |

Shake thoroughly till milky, let stand, filter through moist filter, then add

| | |
|---|---|
| Concentrated alcoholic solution gentian violet, | 10 cc. |
| Alcohol (for preservative), | 10 cc. |

This gives good results but is not very durable, requiring renewal about every ten days. It is best to make the stain freshly in small quantities as needed.

3. Carbolic fuchsin mixture:

| | |
|---|---|
| Fuchsin (basic), | 1.00 |
| Alcohol (absolute), | 10.00 |

Mix, then add

| | |
|---|---|
| 5 per cent. solution carbolic acid, | 100.00 |

This is very satisfactory for many kinds of bacteria, and one of the best for rapid diagnosis of tubercle bacilli, the prepara-

tion being gently heated in this stain till steam appears, washed, excess of color removed by acid alcohol, examined in water or dried and mounted.

4. Carbolic methylen blue:

| | |
|---|---|
| Methylen blue, | 1.5 |
| Alcohol (absolute), | 10.00 |
| 5 per cent. carbolic acid, | 100.00 |

To differentiate, by removing excess of stain, or decolorizing certain forms while others remain colored, the usual fluids are:

Alcohol, 70-90 per cent.
Anilin, with or without xylol added.
Alcoholic solution of acid anilin dyes, fluorescein, tropaolin, eosin.
Acetic acid (0.5 to 1 per cent.) in water.
Iodine-iodide of potassium solution.
Picric acid in watery or alcoholic solution, usually weak.
Mineral acids in water or alcohol (1-25 per cent.).

The first four act gently and leave nuclei and bacteria colored, removing the stain from fibrin, mucus, cell plasm and basement substance; the others act more strongly.

**Cover-glass Preparations.**—With a sterile platinum loop a small drop of the material to be examined (for fluids use the centrifuge and take a little of the sediment) is put upon a clean cover-glass and gently spread in a uniform layer; or two cover-glasses are applied to each other with the material between and gently slid apart. Dry in air with protection from falling dust, or gently over a Bunsen burner; if the latter, holding the cover-glass (smeared side up) in a forceps, describe with it a perpendicular circle of about half a meter diameter, a portion of the downward arc passing evenly through the flame, contact lasting about a second, repeat twice. The best forceps is one which opens only on firm pressure, holding the cover-glass without effort on the part of the user. The heat fixes the albu-

minous matter and the preparation may be stained without fear of washing it off. The stain is dropped on the smeared side from a pipette and if haste is necessary its action is quickened over the flame; then dried and mounted in xylol balsam. Or with a little practice, the cover-glass may be floated on the surface of a staining solution and left there several hours. Löffler's blue is allowed to act in the former case 0.5 to 2 minutes, methylen-blue 3 to 5 minutes; after gentian violet and fuchsin, wash in acetic acid water (1 to 300), then in water, dry in air, mount. Preparations with methylen-blue may be decolorized in equal parts of water and concentrated solution of carbonate of potassium, only the bacteria retaining the stain. After washing, a different stain, as Bismarck brown, may be used for the tissue elements.

5. Gram's Method.

Cover-glass fixed and stained in gentian violet 3 minutes.

Put for 1 to 2 minutes in —

| | |
|---|---|
| Iodine, | 1.0 |
| Potassium iodide, | 2.0 |
| Water, | 300.0 |

Decolorize in alcohol till grayish-yellow, dry and mount: for double staining, after the alcohol use Bismarck brown, wash in alcohol, mount. Acid added to the alcohol hastens its action and prevents precipitation; 3 per cent. HCl or 10 to 20 per cent. acetic. The preparation comes out of iodine solution into pure alcohol, then into the acid alcohol, again into pure alcohol, and double stained as before, though Bismarck brown does not do so well.

This method stains nuclei, bacteria (with exceptions), horny epithelium, mast cell granulations. For a second stain the following is recommended:

6.

| | |
|---|---|
| Fuchsin, | 1.0 |
| Carbolic acid, glacial, | 5.0 |

Rub together till the acid is dissolved, add while steadily rubbing.

| | |
|---|---|
| Glycerin, | 50.0 |
| Distilled water, | 100.0 |

To use, dilute with water to a tenth, stain 1 minute, with gentle heat, wash carefully in water.

The following bacteria are

| *Stained by Gram's Method.* | *Not Stained by Gram's Method.* |
|---|---|
| Actinomycosis, | Cholera asiatica spirillum, |
| Anthrax bacillus, | Coli communis bacillus, |
| Diplococcus pneumoniæ, | Glanders bacillus, |
| Diphtheria bacillus, | Gonorrheal diplococcus, |
| Leprosy bacillus, | Influenza bacillus, |
| Micrococcus tetragenus, | Malignant edema bacillus, |
| Oïdium albicans, | Plague bacillus, |
| Rhinoscleroma bacillus, | Pneumonia bacillus, |
| Staphylococcus pyogenes (all forms), | Pyocyaneus bacillus, |
| Streptococcus erysipelatis, | Relapsing fever spirochete, |
| Streptococcus pyogenes, | Typhoid fever bacillus, |
| Tetanus bacillus, | |
| Tubercle bacillus, | |
| Many saprophytes. | |

**To Stain Spores.**—1. Müller's method.

Cover-glass preparation, dry in air, fix in flame.

Float 5 seconds to 10 minutes on 5 per cent. chromic acid in water; each kind must be tested, anthrax and tetanus require 2 minutes.

Wash in water.

Stain with anilin fuchsin or carbolic fuchsin 1 minute with heat.

Decolorize 5 seconds in 5 per cent. sulphuric acid.

Wash in water.

Stain in aqueous methylen-blue 3 minutes.

Wash in water, dry, mount.

2. Make cover-glass preparation, float on it a layer of Löffler's alkaline methylen-blue, hold over a gas flame and boil, remove for a few minutes and then heat again, wash in water, dip in 95 per cent. alcohol with 0.3 per cent. hydrochloric acid five or six times, wash in water, stain 8--10 seconds in anilin water fuchsin; if successful the spores are blue and the other elements red.

3. Or the cover-glass may be floated on the surface of carbolic fuchsin in a watch glass, this heated to boiling over flame and cooled a little, again heated and cooled a few times; allowed to stand five minutes; placed without washing and charged side up in 3 per cent. hydrochloric acid alcohol and tilted back and forth one minute, double stained with methylen-blue; the spores are red and the other elements blue.

**To Stain Flagella.** 1 *Bunge's Method.*—Prepare a saturated solution of tannin and a solution of 1-20 liq. ferri sesquichlor. in distilled water; to 3 parts tannin add 1 part iron solution; to 10 cc. of this add 1 cc. concentrated watery fuchsin solution — the mordant should be exposed to the air two or three weeks before using. After preparing a cover-glass with a dilute drop of culture, drying in air and fixing in the flame, the mordant is used cold for five minutes and then gently heated a long way above a gas flame; wash in water, dry, stain slightly with carbolic fuchsin and examine.

2. A small drop of broth culture of a flagellated organism, as typhoid, is mixed with 1 cc. distilled water. A drop of this is dried on a perfectly clean slide, high above a flame. A few

drops of night blue solution are allowed to act 8--10 min., and then washed off with water. Stain one half minute in anilin gentian violet, wash and dry. Solutions required:

| | | |
|---|---|---|
| a. | Tannic acid, | 1.0 |
| | Potassium alum, | 1.0 |
| | Distilled water, | 40.0 |
| b. | Night blue, dry, | 0.5 |
| | 95% alcohol, | 20.0 |

a and b are mixed just before using and filtered onto the slide.

Other methods are more complicated; see Löffler's and Van Ermengen's in standard text-books.

**To Stain Capsules.**—Prepare cover-glass, float a layer of glacial acetic acid on it and at once pour it off, drop on gentian-violet anilin water solution and pour off, another dash of stain, again poured off; wash in sodium chloride solution 0.7-1.5 or 2 per cent. (the right strength can be told only after experiment).

**For Staining sections** of tissue to show bacteria, very small and thin pieces must be hardened in sublimate, formalin, or absolute alcohol; imbedded in paraffin; the sections stained by one of the dyes or mixtures given, but for twice or three times as long, perhaps with the assistance of heat (27-40° C.). To differentiate, water with or without acid, anilin and alcohol are used, and also Gram's method; dehydrate in absolute alcohol, clear in xylol, mount in xylol balsam. Counter-staining is often desirable.

# CHAPTER XII.

## TABLES AND STATISTICS.

### The Metric System.

| METER. | GRAM. | LITER. |
|---|---|---|
| 10,000=myriameter | 10,000=myriagram | 10,000=myrialiter |
| 1,000=kilometer | 1,000=kilogram[2]= | 1,000=kiloliter |
| 100=hektometer | 100=hektogram | 100=hektoliter |
| 10=dekameter | 10=dekagram | 10=dekaliter |
| 1=METER | 1=GRAM | 1=LITER |
| .1 =decimeter | .1 =decigram | .1 =deciliter |
| .01 =centimeter[1]= | .01 =centigram | .01 =centiliter |
| .001=millimeter | .001=milligram | .001=milliliter |

EQUIVALENT VALUES.

| | | | |
|---|---|---|---|
| 1 meter, | 39.37 inches. | 1 grain, | 0.065 gm. |
| 1 centimeter, | $\frac{2}{5}$ inch (0.4). | 1 minim, | 0.06 cc. |
| 1 liter, | 1.05 quarts, 2.11 pints. | 1 drachm, | 3.96 gm. |
| 1 gram, or (in most cases) 1 cubic centimeter, | 15.43 grs. | 1 ounce, | 31.68 gm. |
| | | 1 oz., glycerin, | 37.00 gm. |
| 1 milligram, | $\frac{1}{64}$ (0.015) gr. | | |
| 1 kilogram, | 2.2 pounds avoirdupois, 2.7 pounds troy. | | |
| 1 millimeter, | $\frac{1}{25}$ inch (0.039). | | |

To convert grains into milligrams, multiply by 6479.

[1] One cubic cm. of water at its greatest density, 4° C., weighs 1 gm.
[2] One kilo of water at its greatest density, 4° C., measures 1 l.

## Thermometers.

To change Fahrenheit degrees to Centigrade:

Subtract 32, multiply by 5, divide by 9: thus

Normal human temperature, 98.6° F., equals 37°C., for

$$98.6 - 32 = 66.6 \times 5 = 333.0 \div 9 = 37.$$

To change Centigrade degrees to Fahrenheit:

Multiply by 9, divide by 5, add 32: thus

Fever temperature, 40° C., equals 104° F., for

$$40 \times 9 = 360 \div 5 = 72 + 32 = 104$$

| Relative Length of Body Parts. | | | Actual and Relative Weights. | |
|---|---|---|---|---|
| The Body taken as 1,000. | | The Hand taken as unity. | Actual Kilo. | Hand as unity. |
| Body | 1,000 | 8.50 | 64.00 | 118.46 |
| Trunk, | 306.9 | 2.59 | 29.63 | 54.845 |
| Upper extremity, | 501.75 | 4.26 | 3.77 | 6.983 |
| Lower extremity, | 570.3 | 4.85 | 11.14 | 20.62 |
| Head and Neck | 122.7 | 1.043 | 4.56 | 8.44 |

*Example.*—If the hand alone should be found, the probable height of the person from whom it came would be 8.5 times the length of the hand from wrist joint to tip of middle finger, and the weight would approach the weight of the hand multiplied by 118.46: should the headless and limbless trunk be studied the total height would be the excess over the trunk percentage, as above, added to the length of the same, and the weight would be found in a similar way or by rule of three. An upper extremity measuring 29 inches would be 4.26 times the hand; dividing the former by the latter would give the hand as 6.8 inches long; the total height would be 8.5 times this, or 5.78 ft.

These tables, compiled in Germany, are not wholly accurate for the mixed population of the United States.

## THE ADULT SKELETON.—AVERAGE TOTAL WEIGHT 9,814 GM.

| Length in Cm. | Male. | Female. |
|---|---|---|
| Total skeleton | 162-172 | 151-162 |
| Sternum | 18-20 | 16-17 |
| Clavicle | 14.2 | 13.6 |
| Humerus | 32 | 30 |
| Ulna | 26 | 23 |
| Radius | 24 | 22 |
| Hand | 20 | 18 |
| Outer lip of iliac crest to opposite | 28 | 30 |
| Femur | 55 | 43 |
| Patella | 4 | 4 |
| Tibia | 39 | 34 |
| Fibula | 37 | 33 |
| Foot | 24 | 22 |
| Angle between neck of femur and shaft | 127-135° | 112-125° |

## PELVIC DIAMETERS, INLET.

| | Male. | Female. |
|---|---|---|
| Conjugate, | 10.8 | 11.6 |
| Oblique, | 12.2 | 12.9 |
| Transverse, | 12.8 | 13.5 |
| Circumference, | 40.6 | 44.7 |

## NEW-BORN CHILD'S HEAD, DIAMETERS.

| | |
|---|---|
| Fronto-occipital, | 11.75 |
| Biparietal, | 9.25 |
| Bitemporal | 8.00 |
| Mento-occipital, | 12.5 |
| Circumference, | 34.5 |

## THE AVERAGE ADULT ORGANS.

| Organ. | Weight in Gm. | | Proportion to total Weight (assumed as 66.2 K., male, 25 yrs). | Proportion to the New-born as Unity. |
|---|---|---|---|---|
| | Male. | Female. | | |
| Brain | 1,430 | 1,224 | 2.16 | 3.76 |
| Lung, R. | 512 | 458 | 0.77 | 16.97 |
| Lung, L. | 482 | 416 | 0.73 | 20.14 |
| Heart | 300 | 260 | 0.46 | 12.74 |
| Liver | 1,819 | 1,664 | 2.75 | 12.84 |
| Kidneys | 305 | 291 | 0.46 | 13.12 |
| Spleen | 163 | 173 | 0.25 | 15.38 |
| Stomach | 183 | | | |
| Small intestine | 718 | | | |
| Large intestine | 174 | | | |
| Pancreas | 89.7 | | Total weight. | 21.36 |

Specific gravity of normal adult cadaver 0.9213.

## Dimensions of Certain Organs in mm.

| Organ. | New-born | | Adult. | |
|---|---|---|---|---|
| | Length. | Breadth. | Length. | Breadth. |
| Liver | 115 | 88 | 320 | 190-210 |
| Gall-bladder | 32 | | 80-110 | 34 |
| Pancreas | 54 | 20 | 190-220 | 40 |
| Spleen | 40 | 18 | 120 | 75 |
| Thymus | 54-83 | 27-41 | | |
| Kidney | 45 | 27 | 108-114 | 54-63 |
| Ureter | | | 320-340 | |

## Length of Alimentary Canal in cm.

| | New-born. | Adult. |
|---|---|---|
| Incisor teeth to cricoid cartilage | 7 | 14.8 |
| Incisor teeth to cardiac opening | 17 | 40 |
| Stomach | 4-5 | 27-32 |
| Small intestine | 260-350 | 5,650 |
| Large intestine | 42-48 | 160 |

## Capacity in cc. of

| | |
|---|---|
| Stomach, during life, | 1,600-1,700 |
| post mortem, | 2,900 |
| Small intestine, | 6,200 |
| Colon, | 4,850 |
| Urinary bladder, up to | 400 |
| Gall-bladder, | 33-35 |
| Corresponding to | |
| Bile, in grams, | 33.5.-37 |

Skull: adult male, 1,500; female, 1,300

## Dimensions of the Uterus.

| | Virgin. | End of Pregnancy. |
|---|---|---|
| Length | 74-81 mm. | 320 mm. |
| Breadth | 34-45 | 270 |
| Capacity | 3.5-5.0 cc. | 4,960-5,000 cc. |
| Weight | 33-41 gm. | 700 gm |

Placenta, average weight 500-790 gm., usually 75 gm. heavier with boys than with girls.

Total bodily surface, about 1.75 square meters. Pressure of atmosphere upon this surface:

| | |
|---|---|
| At sea level, | 18,000 Kilo. |
| 1,000 feet or 363.6 meters above sea level, | 15,860 |
| At 5,000 feet, | 9,600 |

THE HEART—About the Size of the Individual's Fist.

| Dimensions in cm. | Empty. | Slightly Distended. | At Birth. |
|---|---|---|---|
| Length | 12.9 | 14.9 | 9.0 |
| Breadth | 9.5 | 10.8 | 10.7 |
| Thickness | 6.8 | 8.8 | 3.6 |
| | Male. | Female. | |
| Weight in gm. | 340-375 | 285-300 | 20.6 |
| Proport'n to total | 1:169 | 1:149 | |

DIAMETERS OF CARDIAC ORIFICES IN CM.

| | Male. | Female. |
|---|---|---|
| Aortic | 1.0 | 0.9 |
| Mitral | 1.4 | 1.2 |
| Pulmonary | 1.2 | 1.1 |
| Tricuspid | 1.8 | 1.5 |

The taller the individual the heavier the heart, and the larger the diameters of valve openings.

GREATEST THICKNESS OF WALLS OF CHAMBERS IN CM.

| | Male. | Female. |
|---|---|---|
| Right Auricle | 0.2 | |
| Left Auricle | 0.3 | |
| Right Ventricle | 0.6 | 0.4 |
| Left Ventricle | 1.7 | 1.6 |
| Septum, Ventricular | 0.9-1.2 | |
| Septum, Auricular | 0.25 | |

| | Male. | Female. | New-born. |
|---|---|---|---|
| Total capacity, | 320-380 cc. | 256-320 cc. | 20.6 |

CIRCUMFERENCE OF MAIN VESSELS IN MM.

| | Adult. | At Birth. |
|---|---|---|
| Ascending Aorta | 70-76 | 18-20 |
| Pulmonary | 65 | 23.5 |
| Abdominal Aorta at bifurcation | 32 | |

Daily work of heart, 20,000 kilogram-meters: the kgm. equals one kilo lifted one meter, or 2.2 pounds a little over a yard and three inches.

Total blood in adult 4.5-5 kilo, equals about 1/13 body weight.

Average blood-pressure in large vessels:

| | |
|---|---|
| New-born, | 111 mm. of mercury. |
| At 14 years, | 171 |
| Adult, | 200 |

Time of circulation (adult weighing 63 kilo, pulse beat 72) 22 seconds, or about while the heart beats 26--28 times.

### Dimensions of Red Blood Cell.

| | |
|---|---|
| Average greatest diameter, | 7.74$\mu$ |
| Thickness of edge, | 1.9 |
| Thickness of middle, | 0.99 |
| Superficies, | 128 sq.$\mu$ |

### Blood Cells in Cubic mm.

| Adult. | Male. | Female. |
|---|---|---|
| Red Cells | 5,221,000 | 4,886,000 |
| White Cells | 6,000 | 6,500 |
| Proportion of Red to White | 1:830 | 1:750 |

| | Adult. | New-born. |
|---|---|---|
| Average time required for coagulation, | 9.28 min. | 18.0 min. |

### Nervous System.

| | Male. | Female. |
|---|---|---|
| Brain, average weight in gm | 1358 | 1,235 |
| specific gravity | 1.0386 | |
| breadth of convolutions in mm | 5-17 | |
| depth of fissures | 12-23 | |
| thickness of cortex | 2.94-2.91 | |
| Cord, average length in cm | 44 8 | 41.7 |
| average weight in gm | 39.15 | |
| number of spinal nerves | 31 (rarely 32) | |
| depth of anterior fissure in mm | 2-4 | |
| depth of posterior fissure in mm | 4-6 | |
| Length of spinal column in cm about 2-5 the height. | 69-70 | 66-69 |

## Table of Antiseptic Solutions which Inhibit the Growth of Bacteria.

| | | | |
|---|---|---|---|
| Alum, | 1 part to | 222 | water. |
| Aluminum acetate, | | 6,000 | " |
| Ammonium chloride, | | 9 | " |
| Boric acid, | | 143 | " |
| Calcium chloride, | | 25 | " |
| Calcium hypochlorite, | | 1,000 | " |
| Carbolic acid, | | 333 | " |
| Chloral hydrate, | | 107 | " |
| Copper sulphate, | | 2,000 | " |
| Iron sulphate, | | 200 | " |
| Formaldehyde, pure, | | 25,000 | " |
| Formaldehyde, 40% sol. | | 10,000 | " |
| Hydrogen peroxide, | | 20,000 | " |
| Mercuric chloride, | | 14,000 | " |
| Mercuric iodide, | | 40,000 | " |
| Potassium bromide, | | 10 | " |
| Potassium iodide, | | 10 | " |
| Potassium permanganate, | | 300 | " |
| Quinine sulphate, | | 800 | " |
| Silver nitrate, | | 12,500 | " |
| Sodium borate, | | 14 | " |
| Sodium chloride, | | 6 | " |
| Zinc chloride, | | 500 | " |
| Zinc sulphate, | | 20 | " |

# PART II.—SPECIAL PATHOLOGY.

## CHAPTER XIII.

### CIRCULATORY SYSTEM. I. THE HEART.

**Malformations.**—Two sources of anomalous formation are known, either inhibition of normal development or disease during fetal life.

The heart is at first a straight line, with the primitive aorta at its anterior (or superior) end and the omphalo-mesenteric veins at the posterior (or inferior). Its rate of growth exceeds that of the cavity in which it lies, and hence it early becomes twisted, so that the arterial end lies superficial to the venous. Further twisting and development lead to the formation of the auricles from the deeper limb of the tube, the beginning of the great arteries from the superficial limb, and the ventricles from the middle of the bow joining the two limbs. The tube is made up of an inner endothelial portion and an outer muscular. Septa between auricles and ventricles begin to appear (fourth week) as folds, which meet and become continuous, earlier in the auricles. In the primitive aorta a spirally twisted septum divides the vessel into two more or less triangular blood channels. By the seventh week this division of heart and vessels is about complete.

Commonest among anomalies by defect are imperfect septa and malformed vessels. The entire heart may be lacking or rudimentary, or divided into only two chambers (fish type), or there may be one ventricle and two imperfect auricles (reptilian type), or either septum between the two sides of the heart may

be imperfect, with an undivided truncus arteriosus, or there may be atresia or stenosis of either aorta or pulmonary artery, the latter more commonly affected. Stenosis of the pulmonary, like persistence of the interauricular opening, causes extreme cyanosis, although not incompatible with life, but in the former case the morbus ceruleus is due to general venous stasis, while in the latter it is caused by mixture of venous with arterial blood and may not be very marked. Narrow slit-like communications between the auricles are far commoner than generally supposed and may give no symptoms (25-30 per cent. of all bodies examined). Lastly, the heart, or great vessels, or both, may be transposed, and the abdominal organs may or may not show similar misplacement (situs inversus partialis and totalis). The ductus arteriosus (d. Botalli) may close too soon, from stenosis of the pulmonary, or may persist and is then usually associated with septum defects; the persistence, if the only anomaly present, may depend upon imperfect filling of the lungs, irregular course or unusual diameter of the vessel. The cusps of the pulmonary and aortic valves may be increased or diminished by one. Imperfect development of the anterior thoracic wall or the diaphragm may lead to ectopia cordis though the heart itself is normally developed.

## Disordered Circulation in Heart and Great Vessels.

*Cardiac Thrombosis.*—Cause as for thrombosis elsewhere, slow blood stream, loss of endothelium and roughened surfaces. The first applies especially where there are natural or pathological sinuses or trabeculæ which direct the stream, as in the appendix auriculæ, between papilary muscles, and in aneurysms; the other causes especially with inflammation (endocarditis). Thrombi are found more often in the right side, in the auricles and apices of the ventricles; if between papillary muscles they show root-like processes. If recent they may be loosely attached as a yellowish-white film, if older they become

firmly fixed (organized), the freshest still contain red cells and blood pigment. They form by the collection of leucocytes where the blood stream is slow, then blood plates collect, fibrin is deposited and the color is white, or streaked with red cells and their pigment. These elements, especially the white cells, degenerate and the thrombus may be washed away, or within the thrombus a cavity may form filled with puriform fluid. In the last hours of cachetic patients such thrombi form rapidly and reach a large size; they may be polypoid and fragments may break off and form emboli. In endocarditis small firm white thrombi are often found as vegetations on valves, especially in verrucous endocarditis.

The results of cardiac thrombosis are mechanical interference with the heart's action, narrowing of lumina and impediment to the circulation, embolism of distant arteries, abscess and perforation of the heart wall when the thrombus contains bacteria. Softening or organization or calcification of the thrombus itself may occur, and the latter forms a *cardiolith.*

**Disorders of the Coronary Arteries.**—Protected by the cusps of the aortic valve, embolism seldom occurs. Thrombosis is common late in life and may be the cause of sudden death. Such thrombi form usually where the lumen is already narrowed by sclerotic and atheromatous changes, and the symptoms of this condition, cardiac palpitation, arhythmic and intermittent pulse, angina pectoris, often precede the fatal termination over a period of months. If the thrombus forms very slowly a collateral circulation may prevent serious symptoms till some muscular or emotional crisis ends in sudden death. Although anastomoses occur between certain branches of the coronary arteries, these are so undeveloped that the vessels may be considered as end arteries through most of their distribution. At their origin from the aorta the coronary arteries are often narrowed by atheromatous plates in the aorta and such stenosis may be found even in young persons. Up to a certain degree the heart is tolerant of this condition, but as its nutrition suffers

in proportion to the stenosis, sudden cessation of function may occur at any time. *Infarcts* may occur and lead to rupture of the heart muscle, or such infarcts may be replaced by fibrous tissue and leave depressed and firm scars. The part affected may bulge from the intracardiac pressure, causing chronic aneurysm, and as the left coronary is most commonly affected such changes are usually in the left ventricle.

*Embolism* of the smaller divisions of the coronaries is usually found after ulcerative changes in the aortic cusps, or at times in pyemia, and the heart muscle then contains one or many small abscesses.

When some of the coronary subdivisions are the seat of obliterating arteritis the myocardium presents many areas of fibrous replacement (disseminated fibrous myocarditis).

*Cardiac infarcts* of large extent are usually found near the apex of the left ventricle, either anterior or posterior, and may involve the septum also. The part is pale yellow, dry and of firm consistence at first, afterward softer, at times laminated with alternate healthy and necrosed muscle. Under the microscope there are absence of striation, granular changes in the muscle cells, loss of staining power, hyaline degeneration in the capillaries, fatty degeneration, perhaps pigment and begining limitation by fibrous hyperplasia. Such areas of anemic necrosis may dilate or rupture into the pericardium. If the dilatation is rapid without fibrous repair in the neighborhood it is called acute cardiac aneurysm, if slower with hyperplasia it forms chronic cardiac aneurysm; with the latter, especially, thrombi form on the inner surface.

Simple *anemia* of the heart muscle occurs with general anemia from all causes and is often found in late cachexias; fatty degeneration is usually associated. *Hyperemia* is most often a passive condition and found in the right side of the heart, the veins being very prominent under the pericardium and the muscle a deep brownish-red. *Hemorrhage* is usually small in extent, found about abscesses and infarcts, after vio-

lent deaths as asphyxia of the new-born or from death by hanging, sometimes in septic diseases and valvular lesions and in purpura and the hemorrhagic diathesis. Circulatory disturbances in the pericardium may be acute congestion connected with pericarditis, or with abscess of the myocardium involving the surface, or after sepsis and violent deaths with extreme dyspnea (asphyxia neonatorum). Rupture of cardiac and aortic aneurysms may fill the pericardium with blood, and cause death from pressure upon the heart rather than from hemorrhage; for the membrane is very tough and not elastic and 500-600 cc. of blood within it, whose loss elsewhere would hardly be noticed, will compress the heart and stop its diastole. In general dropsy and pericarditis with effusion a large amount of fluid may collect in the pericardium, but is not so rapidly fatal by compression because of its slower collection and because it does not coagulate.

## Inflammation of the Heart.

Cardiac inflammations may be considered as:

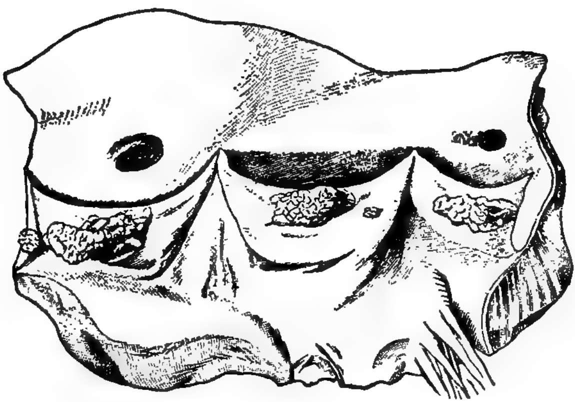
1. Inflammation of the lining membrane, endocarditis
   - verrucous,
   - ulcerative,
   - fibrous.
2. Inflammation of the muscular tissue, myocarditis
   - suppurative,
   - parenchymatous,
   - fibrous.
3. Inflammation of the enveloping membrane, pericarditis
   - sero-fibrinous,
   - adhesive,
   - tuberculous.
   - purulent,

1. **Endocarditis** occurs most often on the surfaces of the valves, may be acute, chronic or recurrent, and is of two chief forms. The warty or *verrucous* is subacute and recurrent, and often the first stage of a valvular lesion. The *ulcerating* or "diphtheritic," causes rapid destruction of the valve, sometimes develops on a verrucous foundation, sometimes appears on

healthy valves, and is the result of bacteria in the blood (mycotic, malignant endocarditis).

*Verrucous Endocarditis.*— The seat is usually the mitral or aortic valve, on the ventricular aspect, less often the tricuspid and least the pulmonary; at times also on the parietal endocardium. The vegetations are fine yellowish-white excrescences, often covered with fresh layers of fibrin, and are made up of spindle-shaped cells derived from the endothelium or from the

FIG. 79.



ENDOCARDITIS VERRUCOSA. (*Ziegler.*)

About the corpus Arantii on each cusp there are fibrous projections and fibrinous deposits on these.

fibrous tissue, with blood-plates and their finely granular detritus between them, leucocytes in varying amount and delicate threads of fibrin. Into the newer layer of fibrin the connective-tissue cells make their way and thus the vegetation continually increases in size. If they do not coalesce the gross appearance is finely papillary, otherwise there are larger and firmer masses, often arranged on either side of the corpus Arantii and from there along the lines of contact (lunulæ) of the cusps. The

process is thus a combined productive inflammation and thrombosis. If the process is rather more acute the organization is less complete, the elements may degenerate and be washed away and only a scar-like thickening remain. If very acute, as may happen at any recurrence, the valve may be destroyed by round-celled infiltration and necrosis and, if not washed away, such parts may be infiltrated with lime salts and variously distorted.

The most extensive changes of this variety occur in the course of acute articular rheumatism and after it, but they are found also with typhoid fever, measles, scarlatina, tuberculosis, pneumonia, and puerperal sepsis. In certain of these the bacteria corresponding have been found in the vegetations, in others the micro-organism is still unknown in the main disease.

*Ulcerative* or *Diphtheritic Endocarditis.*—Probably the initial step in any endocarditis is a superficial necrosis. In the ulcerating form this necrosis is very pronounced and there is deep and extensive ulceration, starting in the vegetations of a previous verrucous form or appearing first as a series of fine yellowish spots on the endocardium, covered with fibrin and degenerating leucocytes. The lesion progresses as a purulent infiltration or as a rapidly spreading necrosis, and, if such dead tissue is carried elsewhere as emboli, it reproduces the purulent or the diphtheritic nature of the lesion. The affected valve may be perforated, or its tendinous cords broken, or large sections may separate and form emboli. The process usually spreads rapidly to the myocardium, especially when the original site is the parietal endocardium, and with this there is almost always suppuration; if the entire thickness of the muscle is involved, purulent pericarditis follows. Emboli occur frequently in the brain (mid. cerebral artery), the kidney, the spleen, and, if the tricuspid is involved, in the lung. Pyogenic cocci, gonococci, bac. coli communis, bac. pyocyaneus, and others have been found in the lesions of ulcerating endocarditis. The clinical symptoms are usually high fever, profound consti-

tutional disturbance, rapidly fatal course and often some clearly demonstrable infection by microörganisms.

*Fibrous* or *Deforming Endocarditis.*—After an acute endocarditis, in old age, or associated with gout and arteriosclerosis, the cardiac valves, especially the aortic, may become thickened, calcified, retracted and stenosed, the cusps of the aortic and the edges of the mitral flaps may be adherent, the chordæ tendineæ of the latter are thickened and retracted, and within the aortic cusps there may be large lumps of lime salts under the endocardial layer. The results are loss of elasticity, rigidity and fixation of the valve segments, narrowing of the lumen, and either *stenosis* or *insufficiency;* for the valve can neither open wide enough to allow the charge of blood to pass from one chamber to another nor close completely and prevent regurgitation. Embolism from deposited fibrin and broken vegetations may follow, and various disturbances of the circulation, with hypertrophy of the muscular tissue from increased effort, and later dilatation.

*Myocarditis* is usually secondary to inflammation of either serous covering, or to stenosis and occlusion of cardiac vessels, or to microörganisms and their toxins in the course of severe general infections.

*Suppurative myocarditis* may follow an ulcerating endocarditis and appear as single or many foci of suppuration throughout the muscular tissues of the heart, the muscle cells undergoing granular degeneration and the intercellular substance tending to loosen about the focus. Such areas of pus formation may follow embolism of the coronary arteries, especially in pyemia, at times also in typhoid fever and inflammatory rheumatism. Here the lesion begins as small points of necrosis, the vessels, as also the affected tissue, containing numerous bacteria. The suppurative process follows the intermuscular connective tissue and forms abscesses, and if these open into the cavities of the heart they are converted into aneurysms by the blood forcing its way into them; even complete rupture of the heart may result in

this way. The abscess may perforate the septum, or open into the pericardium and set up suppuration there.

*Acute parenchymatous myocarditis,* sometimes described as diffuse infectious myocarditis, is one of the well-known lesions occurring in typhoid fever, scarlatina, diphtheria and other

FIG. 80.

CHRONIC MYOCARDITIS. (*Coplin.*)
*m*, muscle fibers undergoing atrophy; *b*, fibrous tissue replacing muscle.

forms of infectious disease. The heart in such cases is remarkably soft and yielding, the right ventricle is apt to be dilated, and the muscular tissue may present faint yellowish-gray mottlings, especially in the portion which works the hardest, the left ventricle. Microscopically such a heart presents a general

granular alteration in all of its cells, and in places this has been succeeded by fatty changes also. Macroscopic tears across the muscle are found and similar lesions are seen by the microscope. Inflammatory infiltration of the connective tissue is almost constant if the case has lasted any time, and the vessels of the deeper layers of the pericardium, sometimes of the endocardium, are surrounded by such infiltrate of small round cells. In more severe cases these are found generally through the tissue. Rounded and spindle-shaped fibroblasts occur in numbers and if the case recovers probably cause fibrous scars.

*Chronic Fibrous Myocarditis.*—When many areas of cicatricial tissue are found throughout the myocardium they may be explained as the remains of infarcts or as due to changes in the coronary arteries, by which the nutrition of the muscle suffers and its cells are replaced by fibrous tissue. A process of this nature may be described as an arteriosclerotic myocarditis and is fairly common as a senile change in the later years of life.

But a similar lesion may occur apart from changes in the vessels, in connection with valvular diseases and hypertrophy, and accompanying syphilis and chronic alcoholism. In such cases there are numerous very fine spots and lines of new connective tissue distributed through the myocardium, making the muscular bundles more prominent by contrast, and the consistency of the organ may be much harder than normal. If degenerative changes have accompanied the process the color is mottled with gray and yellow. Perhaps this is best seen on the inner surface of the left ventricle just below the aortic valve and in the papillary muscles. The entire myocardium may be brownish from the pigment derived from the degenerated cells. Microscopically different portions present various stages of the process, varying from simple and localized infiltration with round cells to relatively large bands of connective tissue, which replace and constrict the atrophied muscle bundles. The lesions may be chiefly about the vessels or apart from their distribution, and with degeneration the cells look granular or fatty. The

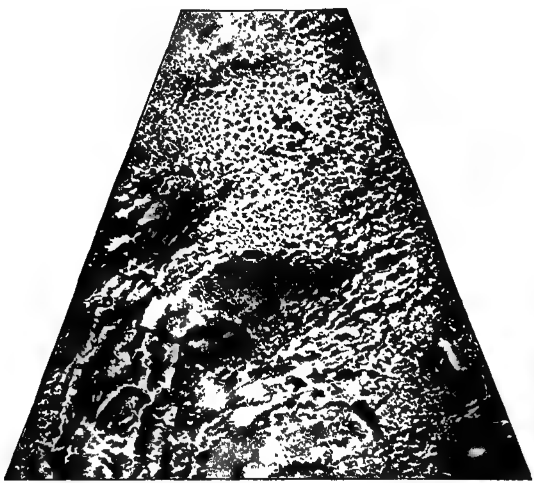
nuclei of the muscle cells are apt to be distorted or swollen. Hyaline changes may be present, and as a rule degeneration and fibrous replacement go on together.

**Pericarditis.**—*The sero-fibrinous form* of this disease usually occurs in general infections but may also follow extension from neighboring parts, as the pleura, myocardium, etc. When pericarditis occurs without general infection, as a single disease, it may be called idiopathic, but even in such cases is to be explained by the microörganisms discovered in the exudate. The disease is characterized by the occurrence of serum in the pericardium in large quantity, and this exudate may be the first and chief lesion or it may precede or follow the production of fibrin on the pericardial layers. Clinically the friction murmurs of the latter condition may often be noted, may then disappear as the fluid accumulates and reappear as it is absorbed. The fibrin is most copious over the heart rather than over the parietal layer of the membrane, beginning at the root of the great vessels as a fine and delicate gray or yellowish membrane, which may at first be easily lifted from the serous surface. During the heart's motion the two layers of the pericardium move so that different areas are in apposition at different times, hence the fibrinous bridges thrown across from one layer to the other are drawn out and frequently broken apart, with the resulting formation of little tags and tassels (cor villosum). In time the fibrin turns a deeper yellow and becomes more brittle. Under it the serous membrane will be found to have lost its smooth and glistening look, appearing more as ground glass which does not permit one to recognize the tissue beneath, and the vessels may be prominent from the inflammatory hyperemia. Under the microscope these vessels are distended, in places irregularly, and surrounded by small round cells. The cells of the serous surface are either swollen and pushed apart by the round cells or entirely lost, and at times the relation of the fibrinous exudate to the vessels is very clear. From the connective tissue of the epicardial

layer a new growth of fibroblasts takes its point of departure, organizing the layer of inflammatory products and carrying the new vessels up into it; from these it is common to have hemorrhages.

*Adhesive pericarditis* (sicca) differs from the preceding chiefly in the absence of any great amount of fluid exudate. The two layers of the pericardium are early united by fibrin

Fig. 81.



Fibrinous Pericarditis. (*Ribbert.*)
The exudate is arranged in fine network and coarser masses.

and these recent and tender adhesions become organized and firm. A similar result may attend the first form after absorption of the fluid. In many cases the two layers do not adhere but the site of the fibrin, which becomes organized, is marked by opaque whitish spots on especially the visceral layer ("milk spots"). Even when the two layers appear to be firmly and wholly united, careful search will discover areas where a lumen persists, still clothed with endothelia. In severe degrees of

obliteration of the pericardial sac, especially when there are recurrent attacks of inflammation, the myocardium beneath the serous layer may undergo marked fatty change.

*Tubercular Pericarditis.*—From an infected pleura, from caseous lymph nodes of the mediastinum and less often from tubercle of the heart wall, the epicardium may become the seat of a typical tubercular inflammation, usually of very chronic course and of the fibrinous type. Pericarditis in connection with other diseases (acute rheumatism) may become infected with the tubercle bacillus later. From the vessels of the imperfectly organized fibrin hemorrhages are frequent. In the exudate the usual elements of tubercular processes are discovered, caseous areas with small lymphoid cells and giant cells and tubercle bacilli.

*Purulent pericarditis* usually follows suppurations in adjacent organs, purulent pleurisy, abscess of the myocardium, perforation of gastric ulcer upward, severe peritonitis carried through the diaphragm, esophageal neoplasms, and pyemic infections. Otherwise it may begin as any inflammation of the pericardium and the exudate becomes abundant and purulent. The myocardium is at once and powerfully affected, becoming edematous and infiltrated with pus in its outer layers, and usually the lesion is rapidly fatal. The collection of pus is often not very large but it may reach such a degree as to distend the cavity and finally perforate, into the pleura of either side or elsewhere.

*Hemorrhagic pericarditis* is simply one of the foregoing with relatively copious bleeding from the newly formed vessels, or develops in the course of some general disease, like purpura and scorbutus, which is associated with frequent hemorrhage.

## Cardiac Hypertrophy and Dilatation.

Three forms of cardiac hypertrophy are sometimes mentioned. These are *simple hypertrophy,* where one or more of the chambers have thicker walls than normally without suffering any

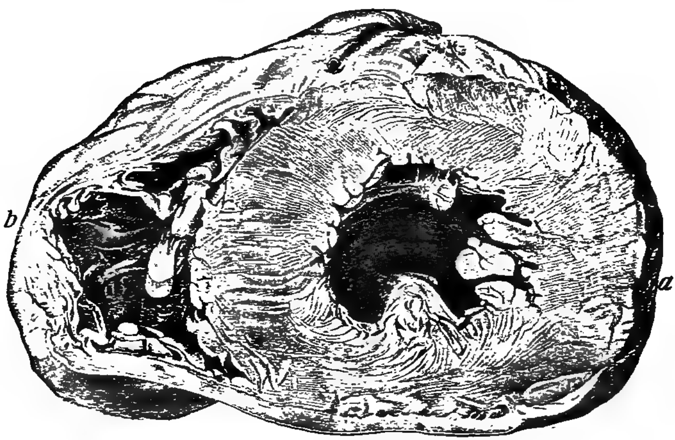
change in capacity; the *excentric*, where the hypertrophy coexists with dilatation, and the *concentric* where the wall is thickened and the cavity diminished. The latter is really a mistaken interpretation of a hypertrophied heart which has stopped in systole and should not be considered as a distinct form.

Cardiac hypertrophy may accompany changes in the valves or the systemic vessels, or occur idiopathically. In the latter case the name simply means that there is no apparent explanation in the vascular system or elsewhere for the increase in size. Such hypertrophy is seen in the heart of those who habitually consume large quantities of beer, in those who have led an especially athletic life, and in those of nervous habit who have through life been afflicted with palpitation of the heart following every slight bodily or emotional effort. In all these cases the heart may later in life give evidnece of being tired out, a presenility due to its excessive functional activity, and in some cases there may be degeneration of the muscle and dilatation of the cavities also. A "normal" size of the heart is difficult to give as it depends so much upon the bodily conformation and the muscular development and activity of the individual, but it bears a certain proportion to the height and a more important one to the weight. In capacity it varies from 150-190 cc. for every 100 cm. of height, hypertrophied hearts reaching 300-400 cc. It weighs 300--350 gm. for the male and 240--250 for the female, all these figures being for the adult. (See Pt. I., p. 328.)

Hypertrophy associated with other diseases may be found in cardiac, vascular and renal affections especially, and in most of the cases is a result of increased work, comparable to any of the voluntary muscles which grow by exercise. From one point of view the heart and the arteries form but one continuous organ, every beat of the former running along the latter to the farthest point where there are circular muscular fibers, and the latter both continue and lessen the work of the heart. Any

change in the vessel walls which impairs their contractility in the same proportion increases the work of the heart, for it can no longer leave to the vaso-motor mechanism the work of carrying the blood wave to distant parts. If in addition the walls of many of the vessels are stiffened, so that friction increases with loss of elasticity, the heart's work is so much the greater, and the part which feels this most constantly, the left ventricle,

FIG. 82.




HYPERTROPHY OF LEFT VENTRICLE. (*Ziegler.*)

*a*, hypertrophied wall of the left ventricle; *b*, wall of the right ventricle. The intraventricular septum also is thickened.

displays the greatest increase in size. This is a partial explanation of the constant hypertrophy of the left ventricle found in renal diseases, for with them there is associated, often over long periods of time, a vascular rigidity throughout the body which enormously multiplies the effort of the left ventricle to send the arterial stream through the system. Hence without valvular changes cardiac hypertrophy and nephritis are commonly associated (see p. 533). A similar explanation suggests

itself for cases where there is general narrowing of many of the vessels, as in senile atheroma, and also where there are dilatations of the larger arteries (aneurysms). When hypertrophy is marked it is termed "cor bovinum." Perhaps the pressure exerted upon the abdominal vessels during the latter months of pregnancy, together with the effort to keep the vascular placenta full, will explain the lighter degrees of the same change commonly found in that condition.

These systemic causes chiefly affect the left ventricle, but similar increase of work for the right side of the heart will give a corresponding hypertrophy of its walls. Very commonly in emphysema, because of the general atrophy of the pulmonary capillaries and consequent increased resistance to the entrance of blood into the lung, the right ventricle shows a high degree of hypertrophy, and similar changes follow chronic pleurisy, fibrous induration and other lung conditions.

In consequence of valvular lesions hypertrophy of the heart is common, and this may follow either stenosis or insufficiency of any orifice or combinations of the same; nearly every stenosis means also an insufficiency of the same valve, but not every insufficience a stenosis. Valvular lesions work in two ways; the arterial side contains too little blood with each systole and the venous too much, whether the lesions be narrowing or insufficience or both. This will be clear if followed out for any one valve and can then be applied to any other. Thus if the mitral be insufficient, at every contraction of the left ventricle some of the blood, which ought all to go out of the aortic valve, will be driven in the wrong direction back through the mitral. Consequently the left auricle contains too much blood and will be distended. The effects of this, as the blood is practically incompressible, are almost like force transmitted through a solid body back through the pulmonary veins into the lung capillaries, and later on through these into the right ventricle. At the same time the ventricle, because of the loss of some of its blood prematurely and abnormally through the

mitral, has too little to contract upon, so that the muscular effort is carried on at a great mechanical disadvantage, the aorta receives too small a charge, and that is abnormally and irregularly delivered. With the diminished supply to the aorta, all the great vessels, and the arterial system in general, contain too little blood while the venous system as a whole is overfilled.

If, on the other hand, the mitral is stenosed, while its insufficence is not yet marked, the ventricle receives in diastole too small a charge of blood, the auricle is constantly overfilled though not subjected to the sudden bursts of the returning column of insufficience, the arterial tree is improperly supplied, and again the tendency is toward venous engorgement and stasis. When both defects are present the disturbance in pulmonary and general circulation must of course be far greater.

Increased work being given to the heart in the above conditions, severe and fatal consequences are delayed only by its ability to meet the added calls, for a time, by increasing the muscular size and power of the cavity walls most involved, and such *compensatory hypertrophy* is most commonly noted in the ventricles, especially the left. The compensation is best attained when the patient has a good general bodily condition and when the valve defect is fairly slow in its development, and so long as the myocardium is normal it is the usual result. The compensation has limits, which are sooner or later attained, and then the hypertrophied muscle ceases to increase still further in size and power, and afterward it passively yields to the internal pressure caused by the obstacle to the circulation, and the cavity dilates. With this there is a rapid and marked loss of power in the heart and a notable increase in the gravity of the symptoms.

An acute dilatation, usually temporary, may follow extreme muscular exertion. With constant severe exercise there may be permanent dilatation with or without hypertrophy.

Valve lesions of the left side of the heart are often associated with changes in the lung from the chronic passive conges-

tion produced (brown induration, pneumonia of heart disease, chronic bronchitis). From the right side, if the blood is obstructed in its passage into the lung, it backs up into the venæ cavæ. Aided by gravity it causes passive congestion of the liver, at times very marked, with atrophy of the cells and fat deposit (nutmeg liver), and various edematous changes are noted in dependent portion (feet and legs).

The gross appearance of the heart varies according to the part involved. When the right ventricle is chiefly enlarged it forms more of the apex than normally and gives a blunt and rounded look to this part. If the left ventricle is chiefly hypertrophied, it presents far more than normally when the pericardium is first opened, the apex is displaced downward and to the left. The organ is heavy in either case but the weight is specially great when both sides are enlarged (cor bovinum, up to 700-800 gm.). In either case the auricles also may be increased in capacity and the walls thickened. The hypertrophied heart is often firmer than normal but the enlarged muscle is really weaker than the normal myocardium. If dilated, and especially with fatty or other degeneration, it may be less firm.

The *stenosed mitral* may resemble a firm white truncate cone projecting into the ventricle, just admitting the tip of the finger or not even so large an object, dense and rigid, the chordæ tendineæ opaque, white and shortened. The *insufficient* mitral admits two or three fingers and while in the opening perhaps they may be separated a little, the valve-flaps are thick, retracted and distorted, and the row of interdigitating nodules along their edges lost in the thickened tissue. The thin fold of endocardium beyond these nodules which normally completes and ensures the closure of the valve is early retracted and lost. The flaps may also be the seat of calcareous deposits and the papillary muscles show fatty or fibrous changes.

On the aortic valve the cusps are thickened, retracted, rigid, infiltrated by lime salts, mutually adherent over a larger or smaller area; both mitral and aortic may be roughened with

verrucous growths and recent fibrin. Similar changes occur to a less degree on tricuspid and pulmonary, the last least often affected. With such valve changes the myocardium seldom escapes, various degenerative changes being present, most apparent when the coronary arteries are also diseased.

Cardiac hypertrophy is in great part a true enlargement of the individual muscle fibers, and of their nuclei also. The connective tissue does not increase in the same proportion and hyperplasia, simple numerical increase of normal muscle cells, plays the least important part.

## Cardiac Atrophy and Degeneration.

Atrophy seldom affects the endocardium except as connected with scars and other results of valvular endocarditis and myocarditis; in the valves small fenestra may be formed in such conditions, but these are usually without significance.

Degenerative changes in the muscular tissue of the heart are of great importance, caused by either local or general disorders.

*Simple atrophy,* or *brown atrophy,* is the result of long-standing processes which affect the muscular cells. Sometimes it appears as a senile change in the very old, sometimes even in early years after long and exhausting disease. In a circumscribed form it may occur in a single ventricle which has first suffered hypertrophy, or about tumors and after myocarditis. Even marked degrees of this degeneration may give no clinical symptoms. Microscopically the individual fibers are noticeably slender, and about the nuclei and in the site of atrophied cells contain numerous fine grains of yellow-brown pigment; where the sheath of the fiber remains it appears as a tube nearly filled with such granules. The pigment is derived from the muscle substance and contains no iron.

An apparent atrophy sometimes may be found in the case of delicate women whose muscular tissues throughout are ill developed, or as part of a general aplasia affecting the circulatory organs.

*Fatty changes* in the myocardium may present themselves as an increase of the subpericardial fat. This is normally found at the base of the organ and along the vessels, but may nearly cover the entire heart and on section be found in the wall even to the endocardium. Such a condition is a replacement of degenerated muscle by fatty tissue, a *fat invasion,* and is a common change in the hearts of beer drinkers and obese anemic women. Such hearts are incapable of much added effort and, if marked in degree, explain some cases of sudden death after muscular and emotional strains.

*Fatty degeneration* of the single muscle fibers may follow local mechanical interference with the blood supply, from pressure upon the vessels by pericardial exudate or thickening of the coronary vessels. Or it may be the result of general conditions, as chronic alcoholism, phosphorus poisoning. Or it may follow acute infectious disease, as scarlet, variola, diphtheria and especially typhoid fever. Certain disorders of the blood may be the exciting agent, and thus it is common in pernicious and other marked anemias and in the cachexias of syphilis, tuberculosis, nephritis.

In the gross the left ventricle shows fine mottlings of a yellowish tinge under the endocardium and when this is limited in degree perhaps the papillary muscles are the site of most evident change; the tissue is soft, friable; the cavities are larger than normal and the heart has stopped in diastole. In very marked fatty change such appearances are repeated in both ventricles and to a less extent in the auricles; at its highest, the knife may even be streaked with a yellowish smear of fat after section of the myocardium. Fatty changes in the heart muscle are very easy to see microscopically, but slight degrees may entirely escape gross examination. Under the microscope a bit of fresh tissue shows loss of striation, though this may persist in many cells, but the single muscle cell is here and there converted into a mass of very finely divided fat granules, which in other places join to form large drops; these may be

arranged in lines following the normal course of the cells. Albuminous degeneration may coexist, which clears with the addition of acetic acid.

Other degenerations may occur in the myocardium, *amyloid* changes in the endocardium and in the vessels, *hyaline* degeneration of the connective tissue, *calcareous* deposits in thickened valves and papillary muscles, but as a general rule these are relatively of little importance.

Various degenerative lesions have been described in the cardiac ganglia, after sudden death in chloroform narcosis and from angina pectoris, either as granular changes in the ganglia with fat formation or as of an inflammatory nature. From their development the cardiac ganglia belong to the sympathetic system, and even if these degenerations are not the result of hardening and staining methods employed, their interpretation remains a matter of uncertainty.

**Wounds of the Heart.**—Penetrating wounds may result from stabs, from bits of broken rib or from foreign bodies in the esophagus. When their main axis runs across the muscle fibers, gaping is marked and blood fills the pericardium at once; running parallel with the fibers and of slight extent they may not permit much bleeding and may heal. Foreign bodies, like bullets, may even become encapsuled in the myocardium. Similar wounds are usually found in the corresponding part of the pericardium. One case is on record where a heavy load of wood coming down a hill pinned a man against a tree trunk, and the heart was found torn from its great vessels and lying free in the pericardium; there was no external wound.

In conditions of marked fatty and other degeneration the heart muscle may rupture, and one form of this is fairly common as accompaniment of the death agony when strong convulsions mark the close of life. Other cases follow myocarditis with abscess, tumor of the heart wall and similar affections. The tears are usually in the left ventricle and disposed across the fibers or in the basement substance. Similarly a

cardiac valve may be torn partially or completely, and those of the left side are more frequently involved than the others.

**Tumors of the Heart.**—Round-celled sarcoma may develop from the connective tissue of the myocardium and occasionally portions of tumor which have been carried in the venous circulation may settle on the endocardium and persist. Cases of lipoma, fibroma, myxoma and a few others have been reported; carcinoma of the breast may pass to the pericardium and the heart itself by contiguity. Almost all such tumors are secondary. Tubercular and syphilitic granulomata are not uncommon in severe cases of these maladies.

## II. DISEASES OF THE VESSELS. ARTERIES.

**Inflammation.**—Acute inflammation of an artery (*arteritis*) usually follows the entrance of foreign bodies into its lumen, either infectious or otherwise, and affects the intima first. The endothelial cells become swollen and their attachment loosened, pus cells appear in the tissue of the wall from the vasa vasorum, and the inflammation extends deeper, to the media or even to and through the adventitia. *Periarteritis* may follow injuries from without or extension from within, and is usually exudative; the vessel at first contracts and lessens its lumen, then as the muscular elements in the media become edematous the vessel dilates. Degenerative changes of part or the whole of the vessel wall follow, thrombi are common. The latter may organize and bring the process to an end or soften and cause embolism of vessels beyond.

*Chronic arteritis* has many names, arteriosclerosis, endarteritis deformans, atheroma and others, and consists in a series of new tissue formation and subsequent or contemporary degeneration; the former affects specially the deeper coats of the vessel, the latter the intima. Such a chronic arteritis may be either diffuse or localized, and shows a tendency to affect certain vessels more than others, as the aorta, the vessels at the

base of the brain, the splenic artery. At times a few of the main trunks are diseased, at times only the smaller divisions, or it may be a general process.

*Diffuse arteriosclerosis* may affect only the arch of the aorta, its commonest seat, or the entire length of thoracic and abdominal portions. From the gross appearance of small roundish or oval plates of thickened and degenerated tissue it has received the name *arteritis nodosa.* These nodules are but little prominent above the general surface of the intima and seem at first to be mere connective-tissue thickenings, and the essence of the process is a replacement fibrosis following changes in the vasa vasorum. These interfere with the elasticity of the media, and because of disturbed nutrition new connective tissue is formed; not being so elastic as the tissue replaced this new connective tissue permits a distention of the media and its own nutrition suffers. Closely connected with this come degenerative changes, often hyaline, sometimes fatty and mucoid. At the same time there is a deposit of calcium salts in the (hyaline) degenerated tissue and such a place projects into the lumen of the vessel and feels of stony hardness. Deeper in the tissue there are little foci of degeneration presenting cell detritus, fat granules, cholesterin tables and salts of lime, the whole being semi-fluid and resembling the contents of sebaceous tumors. This circumstance has given the name *atheroma* (gruel-like tumor) to the process.

The endothelial cells of the intima in such a place are early lost and the intima suffers fatty degeneration. The result is an opening of the vessel which permits the softened material to be swept away by the blood stream, and the remaining cavity is called an *atheromatous ulcer,* though it has but little in common with typical ulcers. Coagulation of fibrin at such a place forms white thrombi and these also contain calcium salts at times. The vessels of the wall are often surrounded by signs of productive inflammation; they may also be increased in number. Fibroblasts and occasionally giant cells are found,

and a scar may replace the ulcer after its contents have been swept away; or the new formed tissue may degenerate in its turn and make the injury worse.

The results of such a process vary with the seat and degree, but if marked there is such an increase in the intravascular

FIG. 83.

ATHEROMA OF AORTA, BEFORE THE ENDOTHELIAL COVERING HAS BEEN DESTROYED. (*Ribbert.*)

The thickening of the wall is most marked about the openings of the intercostals.

friction that the left ventricle hypertrophies. The vessel itself is lengthened and dilated if large, its lumen is usually decreased if small. The thickening is most marked in the intima. Although the muscular elements retain their contractility for a

time, the small artery at last becomes a tortuous stony tube. There appears to be a definite relation between the lesion and points of greatest friction in the artery. From such a stenosis the parts beyond must suffer in their nutrition and in this way senile gangrene may be explained, as well as softening of the brain. If the organs are involved, as the kidney, they become smaller and lose their function. Embolism from fibrin deposits are always possible.

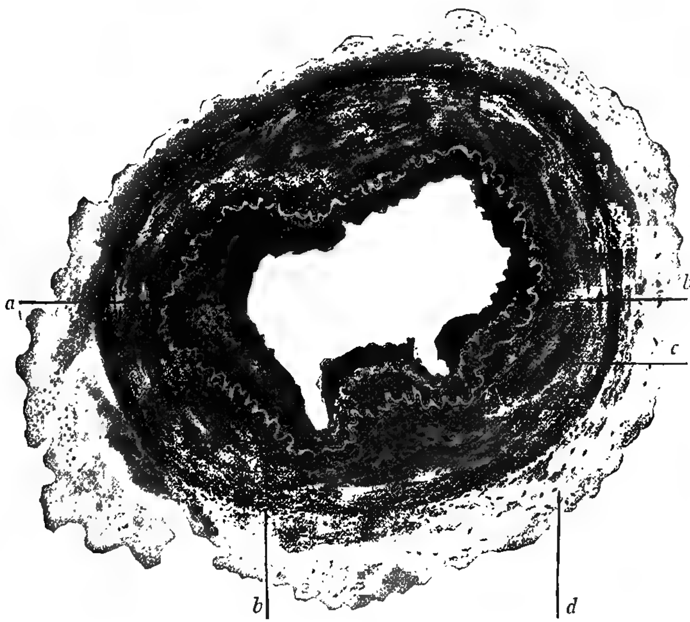
The general tendency in old people for calcium salts to deposit in all tissues, together with decreasing nutrition, explain arteriosclerosis as a senile change; but in addition there are other factors, abuse of alcohol, venereal excess, syphilis, excessive muscular activity, which enter into its production; gout, lead-poisoning and other forms of intoxication also lead to such changes in the vessels.

As a localized lesion chronic arteritis may accompany any productive inflammation (*arteritis obliterans*) which passes over from another tissue and involves the vessel walls. This is common in chronic nephritis, emphysema and tuberculosis of the lungs, and in some lesions of the central nervous system. Certain diseases are characterized by a general tendency to excite new connective-tissue formation throughout the body and of these syphilis and tuberculosis are typical. In the latter case the peculiar structure of the tubercle and the presence of the bacilli are distinctive, but syphilitic lesions are less clearly demonstrated. Gumma may occur in the walls of vessels as elsewhere, starting in them or in the neighborhood. Such lesions have been found in the cerebral vessels, in the carotids and in the portal vein. They differ from atheroma in being confined to one or a few vessels, having less calcium salts deposited, often closing the lumen entirely, and presenting a tough yellowish thickening of either the intima alone or the whole arterial wall. The vessel may be dilated proximal to such a gumma. In the brain, where the clinical symptoms are most pronounced, softening is a common result. Tubercular lesions

are commoner in the veins than in the arteries and will be mentioned in that connection.

Various forms of *degeneration* may be noticed in the arterial walls. Hyaline changes affecting the whole wall are common in various organs with inflammatory processes, as in the glo-

FIG. 84.




ENDARTERITIS OBLITERANS. (*Coplin.*)

*a*, intima thickened and thrown into folds; *b*, elastic coat; *c*, media, irregularly thickened; *d*, adventitia.

meruli with nephritis, also in the walls of aneurysms and in vessels closed by thrombi, and it is often the first stage of arteriosclerosis. It appears as a homogeneous and structureless substance replacing the elements of the vessel wall. Fatty degeneration occurs in both intima and media, with chronic arter-

itis and independently, appearing in the gross as fine yellowish dots and lines under an endothelium which is clouded. Microscopically the fat granules and drops are found within the cells, muscle and other, and afterward between them also. From the internal pressure such a weakened spot yields slowly, forming an aneurysm, or suddenly after great increase of the stress. Deposit of lime salts in the arterial walls accompanies certain chronic bone disease with absorption of the lime, the material being laid down again in the vessels. Sometimes it appears without evident cause, especially in the arteries of the uterus, the abdomen and the legs. Amyloid degeneration especially affects arteries, and of them particularly the smaller divisions; by treatment with iodine they appear as brownish twigs and branches.

**Aneurysm.**—Dilatations of arteries in which one or more of the coats are involved are called *aneurysms*. If a wound of the vessel has allowed the blood to escape into surrounding tissues, and it is confined there, it may be termed *aneurysma spurium* or *false aneurysm,* and in the recent state this is diffuse; in older and encapsuled collections it is circumscribed. In the latter case the vessel may still communicate with the hematoma and then the resemblance to true aneurysm is very close.

*Dissecting aneurysm* is the name given to vascular dilatations which have arisen from tears in one coat (intima) or occasionally in two (media also), which allow the blood to force a path along the vessel between its layers, making fusiform swellings along a portion of the artery. Such a collection may force its way out into the tissues or back again into the vessel. Dissecting aneurysm is most common in the large vessels and perforates in the direction of least resistance, into the pericardium frequently. In the brain the blood may pass out of the vessel entirely but be confined within the periarterial lymph channel. Dissecting aneurysm is most commonly caused by violence, but may occasionally follow disease and degeneration in the vessel wall.

*True aneurysm* is the local dilatation of an artery in consequence of weakened resistance in its walls, the blood-pressure forcing the weaker part outward. Either at first or as a result of the stretching, there is a sòlution of continuity in the intima, then in the media, less often in the adventitia. The commonest form of true aneurysm is the *sacculated,* where the dilatation is lateral, spheroid, not involving the entire circumference of the vessel; often seen on arteries which are arched and then on the convex aspect. Other forms are the *diffuse,* a relatively long section (entire thoracic aorta) being uniformly dilated, and the *fusiform,* where a shorter length is involved and the spindle shape is more evident. Combinations of one or more are common.

Once formed, the aneurysm may persist for a long time with but little change. Internally thrombi slowly form in layers, soft parts in the neighborhood accommodate themselves to the pressure. Hard structures, as bone, are slowly eroded by the steady pressure, because at that point the vessels of the periosteum are occluded, and hence it atrophies. The continuous deposit of layers of thrombus may lead to healing of the aneurysm if the opening into the vessel is small and the adjacent wall fairly healthy. Otherwise, in spite of the stratified clots, the aneurysm bursts and a hematoma forms in the tissues, or a cavity is filled by the rapid bleeding with fatal consequences.

*Aneurysma verum* has sometimes been termed spontaneous, but this adjective can have only the signification of non-traumatic in such a case, for the dilatation is always preceded by inflammatory or degenerative changes or both in the vessel wall, and a healthy artery cannot dilate spontaneously enough to form an aneurysm. The essential feature of any such lesion of the artery, leading to formation of an aneurysm, is that the elasticity of the media is decreased and consequently its resistance. The common explanation of aneurysm, that atheroma makes a solution of the intima and allows the blood to exert pressure on a (relatively) healthy media and thus dilates the

vessel, cannot be admitted as the only one, otherwise aneurysm from nodose atheroma of the aorta would be a more frequent post-mortem find. The common appearance of atheroma without aneurysm and of aneurysm without atheroma, refers the production of the dilatation to some less evident etiology. Perhaps it is closely connected with congenital imperfections in the

FIG. 85.

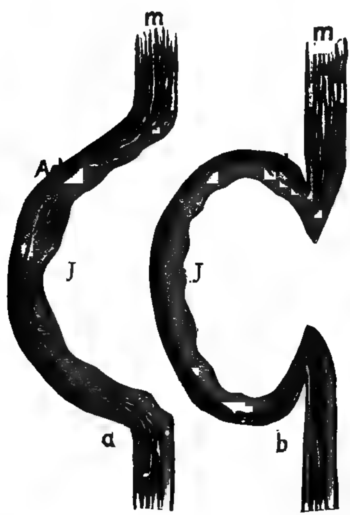



DIAGRAM OF THE ARTERIAL COATS IN AN ANEURYSM. (*Ribbert.*)

*J*, intima; Ad, adventitia; these are continuous in the sac; M, media, can be traced in *a* and in the lower part of *b*.

development of elastic tissue generally, and a side light is thrown upon the subject by the occurrence of emphysema in certain families. Here the elastic tissue of the lung is at fault, and if the influence of heredity may be admitted to explain its causation, perhaps a similar hypothesis will hold good for aneurysm.

Aneurysm is commoner in men than in women, in certain countries (as England) more than in others, and in the ten years from 35 to 45. Although the chief danger of an arterial dilatation, namely its rupture, usually coincides with some great muscular effort and consequent increase of intravascular pressure, it is interesting to note that quite frequently aneurysms break while the individual is asleep; the medico-legal importance of this may be critical.

If the wall of the aneurysm is formed by very slow dilatation it may consist of all three coats, but in most cases the elastic and muscular elements are entirely absent and sooner or later the intima also. One form of multiple congenital dilatations is common about the bifurcation of small vessels, and here the elastic tissue is wholly lacking while the muscle cells are few and imperfectly developed. A form of rapidly developed aneurysm depends upon suppurative and other changes in the vessel wall, derived at times from the neighborhood, at times from septic emboli; the emboli are occasionally parasites or fragments of them, eggs, etc. A form of multiple miliary aneurysm occurs in the brain and leads to cerebral hemorrhage, especially affecting the smallest arteries and of these the branches of the lenticulo-striate most commonly. They are due to degenerative changes in the media, as elsewhere, though often associated with atheromatous and vaso-motor lesions.

The large vessels vary in their disposition to aneurysm, the thoracic aorta being by far the commonest seat, followed by the popliteal, the femoral, the abdominal aorta, the carotids, the subclavian, etc., in the order of frequency.

**New Growths.**—Hypertrophy of large sections of the arterial tree may accompany similar change in the heart. Tumors formed of new and dilated arteries occur, and similar elements are found in many other neoplasms. Tumors may attack the artery from without, involving the adventitia, but seldom the media; at times the endothelium proliferates even though the media remains uninfluenced by such an attack, giving rise to

endothelioma and combinations. Or the vessel may become the seat of a neoplasm from embolism of small portions of the new growth, the endothelium growing into and continuous with the embolism or replaced by its cells. As a general rule the vascular wall exhibits a high degree of resistance against tumors growing in the neighborhood. New vessels formed in tumors seldom reproduce the normal type of structure, especially in sarcoma, where the blood circulates through simple channels in the neoplasm.

## Veins.

**Thrombosis.**—The coagulation of the blood within the cavity of a vein may occur from many causes, and varies in results according to the size of the vein, its anatomical site and relations, and the septic or aseptic nature of the thrombus. General aspects of the subjects have been dealt with in the first part (see Pt. I., p. 40). Special features of individual veins may be inferred from their relations and the ease of establishment of collateral circulation.

**Inflammation.**—*Phlebitis* is described as peri-, meso-, or endophlebitis according to the position of the inflammatory process in the wall of the vessel. If caused by inflammation in adjacent tissue it usually begins as periphlebitis, if from a septic agent within, as an endophlebitis. It may be an acute infectious inflammation, frequently of a superficial vein and following injury. The anatomical steps are first a round-celled infiltration of the adventitia which may go on to be purulent. This process follows the course of the vein and makes smaller or larger abscesses, combined with thrombosis of the contained blood as soon as the wall of the vein is severely involved. Such thrombus formation for a time prevents the access of pus and pyogenic organisms to the general circulation, but at last the thrombus also may be destroyed and the infectious material is able to enter freely. With the latter, multiple septic embol-

ism is the natural result: if such entrance is prevented and the course of the inflammation is favorable the thrombus may organize and the lesion heal.

Suppuration in the course of the portal vein is called *pylephlebitis* and follows pyogenic infection of any of the general or hepatic branches of the vein. Thrombosis and purulent softening occur, the vein in a great number of its branches is filled with a puriform fluid, such branching abscesses reach all through the liver, and the inflammation may pass from the vessel to other tissues. Capillary stasis and thrombosis occur throughout the territory of the branches of origin, causing hyperemia and loss of function in the organs involved. The disease may be rapidly fatal or last for a week or more.

Phlebitis occurs also in chronic forms and is sometimes called *phlebosclerosis* because of its resemblance to arterial sclerosis. Slight and localized forms may generally be found in connection with dilated veins and slowed blood current in varix, the veins being increased in thickness and distorted. As a general condition it may accompany arterial sclerosis or rarely occur by itself. The veins of the lower extremity are especially liable to such thickening and show in the gross small scattered areas of denser tissue, due to round-cell infiltration, hyaline degeneration and productive change of all the elements of the wall. At times there are no gross evidences though the microscope reveals those mentioned.

**Varix.**—Dilatation of a vein may affect the vessel just above a valve, which then may become incompetent or torn off, or it may involve a long stretch of the vessel, tapering to each end and giving the fusiform phlebectasia. In more marked cases the vessel is elongated and very tortuous (cirsoid form), or on the side of the vessel, similar in form to the sacculated aneurysm, there are few or many protrusions. These may press against each other and become continuous by atrophy of the walls at the point of greatest pressure, so that the appearance of erectile or cavernous tissue is reproduced. Thrombi may

form in such dilated spots and by the deposit of lime salts become converted into phleboliths. Such a process is common in old age in certain venous plexuses, as the prostatic. Periphlebitis may follow or the phlebolith, which acts as a foreign body, may become encapsuled and separated from the vessel in which it is formed.

The section whose circulation is interfered with as the result of such varices and phlebectasias will suffer in varying degrees according to circumstances: usually edema is marked, a mucous surface is the seat of chronic catarrh, a skin surface as on the legs becomes the seat of chronic ulceration with eczematous and other complications. These varicose ulcers heal with difficulty on account of the imperfect nutrition of the part, and break down again readily; pigmentation is common. The skin may also be the seat of productive fibrosis and be many times thicker than normal, its surface creased and folded or warty and cracked, with passive serous exudation. The clinical appearance resembles elephantiasis and is often complicated with eczema and ulceration. The floor of varicose ulcers is apt to become very hard and cicatricial. The veins may be opened by ulceration and severe bleeding result.

The two main factors are mechanical interference with the return flow of blood and pathological changes in the venous walls. The former is seen in parts where physiologically a long column of blood tends to dilate the veins passively by its weight, as in the scrotum and on the legs, and also with the results of pressure in the abdomen from enlarged uterus, chronic constipation, and the increased resistance to the venous current resulting from emphysema and cirrhosis. Disease of the vessel wall is almost constant; some form of sclerosis which lessens its resisting powers. Certain forms of dilated veins have received special names, *varicocele* if the spermatic veins are dilated, *hemorrhoids* if those about the lower end of the rectum, *caput medusae* if the superficial abdominal veins dilate to relieve the obstacle in the portal vein caused by atrophic cirrhosis and tumors of

the liver. Phlebosclerosis and varix usually coexist, but either may be found apart from the other.

**Neoplasms.**—Primary tumors of the veins, as of the arteries, are among the pathological rarities. Secondarily they may be involved by any tumor, especially by malignant forms, and the veins possess less resisting power than the arteries. Local dilatations, or tumor masses formed of such dilated veins, are common in the liver under the name of angioma. Infectious granulomata may affect veins, especially tubercle, and such a hidden source for rapidly generalized tuberculosis must always be kept in mind. Thus a superficial vein may be involved from a caseous lymph node, and such venous tubercles are very common in the vessels of the lung. Syphilis may appear congenitally in the portal and other veins, and later in life gummata occur here as elsewhere.

**Lymphatic Vessels.**—Inflammation of these vessels is called *lymphangitis* and may be either simple or septic. It follows superficial wounds with loss of substance and presents itself as a red line of hyperemia along the track of the vessels involved, progressing till the nearest node is reached, which then swells and becomes tender. If septic, the node is apt to suppurate and form an abscess and smaller abscesses may be formed along the course of the vessel. The organisms recovered from such inflammations are the pyogenic cocci, aureus, epidermidis albus and others. Severer grades of such inflammation lead to the development of large phlegmonous abscesses and regularly occur with serious post-mortem and dissection wounds. Such lymphangitis is especially apt to follow injuries received at autopsies made very soon after death, in cases of infectious disease, puerperal fever, etc. At times it begins as an infection of the lanugo hair-follicles (sycosis) and so passes through the unwounded skin.

Dilatation of the lymph-vessels is not so common as in the blood-vessels. The causation resembles that of varix, an ob-

stacle to the centripetal current passively blocking and dilating parts more distally placed; previous weakening of the wall by inflammation plays a part here also. Such lymphangiectasis is common in elephantiasis Arabum (see Pt. I., p. 672). Tumors and scars which lessen the lumen of a chief lymph-vessel (as the thoracic duct) may produce lymph stasis distally, and through any defect in the surface there may be an outpouring of lymphatic fluid (lymphorrhagia). This is usually white and opaque, like milk, and contains many fine granules of fat and a few white cells. In the peritoneal cavity a collection of such fluid is called chylous ascites. Certain parts especially are apt to be the seat of lymph stasis, with thickening of their elements or hypertrophy and exudation of lymph; among these the scrotum, labia and thigh may be mentioned.

The relations of the lymph channels to tumors is important in two ways. A tumor formed of newly developed lymph-vessels is called a lymphangioma,—*simplex* when they are not very much enlarged in caliber, *cavernosum* when dilated; the latter form is usually a congenital condition affecting especially the upper end of the alimentary tract (macroglossia). *Lymphangioma cysticum* is a similar tumor with very wide lymph-vessels and occurs at times about the neck and the sacral region; the contents of the cysts is usually very fatty, at times partly coagulated. Certain forms of endothelioma begin in the lymph spaces of various tissues, often on serous surfaces. The second important relation of lymph-vessels is as the way along which malignant tumors spread, particularly carcinoma; this is a fact of the utmost practical importance clinically, in all operative procedures on malignant tumors (Pt. I., p. 178).

Infectious granulomata regularly involve the lymph channels, tuberculosis especially, as seen in tubercular ulcers of the intestine; and syphilis, in nearly all of its stages, affects the superficial and deep nodes. Doubtless both diseases spread frequently along lymph channels.

## The Blood.

**Physiology and Morphology.**—Specific gravity: normal 1.054-1.060. It is increased with muscular activity, menstruation, high altitudes, skin lesions, and in the new-born; decreased in chlorosis, simple and pernicious anemia, leukemia, and with malignant tumors.

**Red Cells.**—Average diameter 7--8 $\mu$; achromatic while living, acidophile when fixed; considered as vesicles containing semi-fluid contents or as viscous solid masses with an elastic stroma which is condensed peripherally. Variations in size include: *Microcytes* from 4 to 1 $\mu$ in diameter, in chlorosis and pernicious anemia, with deficient hemoglobin. *Megalocytes,* 10--20 $\mu$, hemoglobin increased or diminished, in severe grades of anemia. *Poikilocytes,* various pear-shaped and distorted cells, in severe anemia with degenerative changes in the red cells. Nucleated red cells occur as *normoblasts,* 7-8 $\mu$, in various anemias; their presence regarded as reparative; *megaloblasts,* 10--20 $\mu$, the nuclei single or multiple, may show mitosis and fragmentation (karyorhexis). Over 20 $\mu$ in diameter they are called *gigantoblasts.* Presence indicates pathological cell formation in the marrow. occur in primary and secondary pernicious anemia.

*Number.* 5 million in males, 4 million and a half in females, in the cubic millimeter; varies with time of day, digestion, sex, menstruation, pregnancy, and nervous disorders. Increased (relatively) in profuse discharges from bowels, endocarditis and venous stasis, phosphorus and CO poisoning; condition termed *polycythemia.* In hemorrhages the number diminishes: *oligocythemia.*

**White Cells.**—Average number in cu. mm., 8-10 thousand; normal varieties (after staining):

1. *Lymphocytes*—about the size of red cells, as flat objects present narrow basophile rim, homogeneous or reticu-

lated, about compact or reticulated spherical nucleus; granules absent but reticulum may show nodal thickenings; no nucleoli. Vary from 22 to 25 % of total white cells.

2. *Large* mononuclear leucocytes, may be largest cells in normal blood, protoplasm slightly basophile, finely reticular with nodal thickenings; nuclei vesicular, circular, horseshoe or elongated, coarsely reticulated. From 2-4 %.

3. *Polynuclear,* two or three times diameter of red cell, protoplasm reticulated with neutrophile granules, reticulum itself slightly basophile; nuclei elongated and constricted into two or more lobes with connecting threads of chromatin, coarsely reticulated with central nodal thickening. 70-72 %.

4. *Eosinophile,* vary in size, protoplasm contains granules which are strongly acidophile; nuclei bilobed usually and coarsely reticular. 2-4 %.

In pathological blood occur also:

5. *Myelocytes* with neutrophile or eosinophile granules, mononuclear, in three forms:
   (*a*) Ehrlich's myelocytes, medium size, nucleus central and pale, neutrophile granules; in leukemia and secondary anemia.
   (*b*) Cornil's myelocytes, larger than No. 3, nucleus eccentric and pale, granules neutrophile; in myelogenous leukemia.
   (c) Eosinophile myelocytes, like No. 4 but nuclei single; in myelogenous leukemia (granules may be excessive in size), malaria, myxedema.

6. *Mast cells,* mono- or polynuclear, contain large and small strongly basophile granules, metachromatic with many stains (thionin); in myelogenous leukemia.

The behavior of these cells with various stains is important.

Anilin stains may be divided as follows (Ehrlich):

1. Basic stains, which unite as bases with the acid principles of cells (nucleinic acid); in the order of selective power, hematoxylin, methylene blue, thionin, etc.
2. Acid stains, which unite with basic principles in cells, as eosin, fuchsin, aurantia.
3. Neutral stains, usually mixtures of the two previous kinds, which show affinity for certain parts of cells, as artificial indigo (from propiolic acid) and the "triacid" stain.[1]

Classified according to the reaction of their granules leucocytes may be divided into:

A. Basophile, including mast cells, lymphocytes and large mononuclear leucocytes.
B. Neutrophile, polynuclear leucocytes, myelocytes.
C. Acidophile, eosinophile, leucocytes and myelocytes.

*Variations in Number.*— Excess of polynuclear cells is called *leucocytosis* with or without the word polynuclear prefixed; if more than one kind, *mixed leucocytosis;* excess of lymphocytes, *lymphocytosis;* of eosin cells, *eosinophilia.* Physiologically there is leucocytosis in the new-born, after ingestion of food and during pregnancy. Pathological leucocytosis occurs with fever and inflammation, after hemorrhage, in cachexias and just before death.

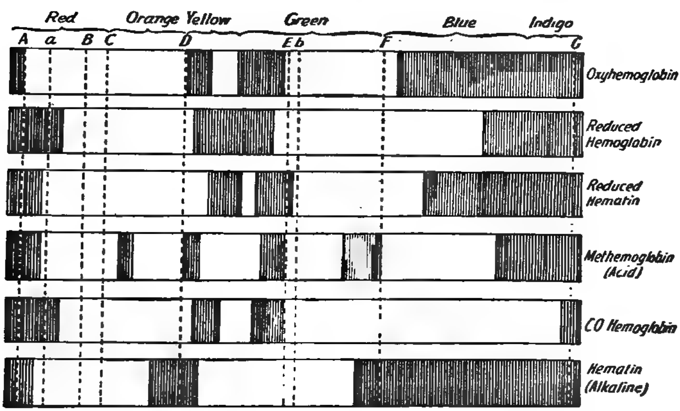
**Blood Plates.**—These are oval or circular in outline, colorless, homogeneous or granular, 1--3 $\mu$ in diameter, and stain with acid and basic dyes. They are cohesive, of relatively high sp. gr., and are supposed to aid in formation of fibrin (coagulation). The number is estimated at 180,000 to 500,000 per cu. millimeter, and they are supposed to increase in non-

[1] Ehrlich considers the basic dyes as chromatin stains, the acid as plasma stains, and the neutral as given above; but the method of use and other considerations modify these views. For instance, orange and acid fuchsin are acid dyes, but by regressive staining they may color chromatin as well as plasma, safranin and nigrosin stain plasma though basic, when used with mordants. (Lee, M. V .M., p. 194.)

febrile anemia, leukemia and hemorrhage, to decrease in fever, malaria and after poisons. Their exact significance is unknown, but their origin (perhaps not in all cases) is from extrusion of chains of globular material by red cells; this material gives some of the reactions of nucleo-proteids.

**Hemoglobin.**—The estimate of this body is of importance in anemias and certain poisonings. It may be accomplished in one per cent. solutions by the spectroscope, which shows both the blood pigment and also its particular form. Blood

FIG. 86.




SPECTRA OF BLOOD PIGMENTS.

recently clotted may be dissolved in water; older clots by erated in ammonia, with the reduced or alkaline hematin spectrum. Clots which have been exposed to heat should be macerated in ammonia, with the reduced or alkaline hematin spectrum resulting.

In fresh blood with the hemoglobin (Hb) unaltered, the spectrum of oxyhemoglobin is obtained, with an absorption band at *D*, rather thin, near the orange, and another at *E*, broader, near the green. The indigo and most of the blue are

absorbed. With the addition of reducing agents (as ammonium sulphide) the color of the fluid darkens and the spectrum shows a broad band between *D* and *E*, less absorption at the blue end and more at the red — the spectrum of reduced hemoglobin. This test is positive indication of the presence of blood.

Hematin is produced by the action of acids and strong alkalies on reduced Hb. In acid solution its spectrum is similar to that of acid methemoglobin; in alkaline, it gives a broad band at *D*.

Blood containing methemoglobin may be chocolate color in the gross. Its spectrum in acid or neutral solution gives four absorption bands, one quite sharp between *C* and *D* in the orange, a fainter band in the yellow to the right of *D*, a broader band, more distinct, to the left of *E*, a fourth band to the left of *F* which may merge with complete absorption of the blue end. Carbonic oxide hemoglobin gives a rosy or cherry red color to both venous and arterial blood. In .5 per cent. dilution the spectrum resembles that of oxyhemoglobin but the bands are broader, the *D* band is displaced to the right, and there is less absorption at the blue end. On addition of ammonium sulphide to normal blood the spectrum of reduced Hb is obtained, that of CO-Hb remains unaltered. Corroborative tests should be used:

1. Warm the specimen with 10 per cent. solution of NaOH; normal blood becomes brownish green; CO blood turns cloudy, then clear red, with red flakes on the surface.

2. Zinc chloride solution colors normal blood black; CO blood bright red.

3. Dilute 4--5 times with lead acetate; normal blood becomes chocolate colored, CO blood red.

The estimation of the percentage of Hb in blood requires special apparatus and training. Miescher's modification of Fleischl's hemoglobinometer is as accurate as any and its technical difficulties trifling.

## Special Pathology of the Blood.

**Chlorosis** is a disease which occurs chiefly in young women from defective hematogenesis, affecting principally the hemoglobin and secondarily the number of red cells. Arterial hypoplasia, auto-intoxication and functional nervous disorders have been supposed to favor it; heredity, poor hygienic surroundings and the establishment of menstruation are important; with the predisposition, an imperfect absorption of iron exists.

*Blood Changes.*— Total blood perhaps reduced (oligemia), sp. gr. diminished in proportion to the loss of Hb, low Hb index constant, in average cases Hb ranges between 35 and 45 per cent., index about .5; red cells slightly reduced, may be variations in size and shape, poikilocytes in severe cases and also nucleated red cells.

**Progressive Pernicious Anemia.**—This name includes all grave anemias in which the megaloblasts exceed the normoblasts or at least 33 per cent. of megalocytes are present (less in remissions). Its causation is undetermined (cryptogenic) in many cases; others coincide with chronic gastritis, gastric carcinoma, intestinal parasites (bothriocephalus latus, anchylostoma), repeated hemorrhages, and pernicious malaria, syphilis, prolonged diarrhea, typhoid and yellow fever. The essential lesion is metaplasia of the lymphoid marrow with production of megaloblasts; such metaplasia is invariably present, may resemble tumor formation, and is pathognomonic. The lesion in the blood is defective formation of cells and their destruction by some hemolytic agent.

*Blood Changes.*— Red cells from 1,000,000 to 200,000, megalocytes with increased Hb from 33 to 90 per cent.; megaloblasts very scarce, or numerous or outnumber normoblasts; microblasts rare. In fresh blood coagulation is feeble, rouleaux of red cells do not form, ameboid movement of poikilocytes may be present, of microcytes usual; degenerative altera-

tion of red cells common. Leucocytes reduced, number may rise before death. Sp. gr. as low as 1.027.

**Leukemia** is regarded as a primary disease of the blood-producing organs principally affecting the marrow and the lymphoid structures. The essential process consists of hyperplasia of myelocytes or lymphocytes, or both varieties of cells, with secondary increase in leucocytes, and secondary lesions in viscera; it leads eventually to disturbances of red cell production and pernicious anemia. In the myelogenous type the marrow and the neutrophile myelocytes are chiefly involved, in the lymphogenous type the lymph nodes, spleen and lymph cells of marrow are most affected and red cells suffer less early. The types may be mixed, as the disease affects one or the other group of structures at different stages. The apparent resemblance between leukemia and neoplastic formations, and cases of lymphemia arising in connection with lympho-sarcoma, are of great but still undeciphered interest. (See p. 430.)

*Blood Changes.*—But slight alterations in bulk, color usually pale, coagulates slowly (at autopsy), the red cells settling and leaving white cells and fibrin in a thick layer above them, with clear serum above all.

Red cells reduced to two or three millions or lower, deficient in Hb, size uniform, rouleaux normal, normoblasts fairly numerous, smear on slide peculiarly opaque and granular from excess of leucocytes. In late stages red cells show alteration in form with degenerative changes. Hb lower than normal.

White cells increased to 100,000--200,000 or more. Neutrophile forms occur as large mononuclears with central well-staining nucleus, abundantly present, and as large myelocytes with pale eccentric nucleus. They may be lacking in neutrophile granules or show hydropic degeneration of the nucleus. Polynuclear neutrophiles occur from 17 to 72 per cent. (average 46 per cent.) and seem to vary inversely as the myelocytes; in the lymphatic form of leukemia they are very scarce. Degenerative changes in these cells are common; increased cohesive-

ness, paleness of nuclei, fragmentation of nuclei, and hydropic swelling. Eosinophiles are increased in the myelogenous form, varying from 3,000 to 100,000, hence the diagnostic value; ameboid movement well marked. In acute leukemia of both types, and in chronic lymphocythemia they may be very scarce. Eosinophile myelocytes with granules of unequal size and staining affinity are pathognomonic of myelogenous form. Lymphocytes vary in numbers and proportion, but are less in proportion as the myelogenous character of the disease prevails. They vary from 2 per cent. to 10 per cent. Large mononuclear leucocytes occur but seem to lack significance. Degenerative changes are common in these cells. Mast cells are more numerous than normally but may require search; they may exceed the eosin cells.

*Special Characters of Blood in Lymphatic Leukemia.*—The lymphocytes are the only form of white cells appearing in increased numbers and in some cases determine the nature of the disease without question; but the causes of chronic leucocytosis are so numerous that caution is necessary. They are usually of small size and normal structure and may attain 80-90%. In rare cases they may be large, especially in children; in chronic cases and adults the small prevail. Myelocytes, mast-cells and polynuclears may be very scarce, nucleated red cells are scanty.

Both the numbers and the proportion of white cells may vary much in the course of the attack, owing to intercurrent disease. Spontaneous changes also occur and the disease may pass into pernicious anemia, just as pseudo-leukemia may pass into true leukemia.

The sp. gr. may be reduced with loss of Hb or restored by other albumins; alkalinity may be diminished, fibrin may be present in excess, peptone, nuclein, xanthin and uric acid have been found in the blood by various observers. Charcot-Leyden crystals are present in the blood during life and in all tissues (spleen) and exudates after death.

**Pseudo-leukemia** (Hodgkins' disease) differs from leukemia in the absence of marked leucocytosis and in the hyperplasia of all lymph tissues, with metastatic growths in various organs. The anatomical lesions have included simple inflammatory hyperplasia of lymph nodes, lymphadenoma, and lympho-sarcoma. Until the etiology is definitely ascertained, the transitions be-

FIG. 87.

HODGKIN'S DISEASE. (*Coplin.*)
Cervical and axillary nodes enlarged.

tween pseudo-leukemia, and hyperplasia of lymph nodes, leukemia, lympho-sarcoma and pernicious anemia, seem to indicate that they are closely related and perhaps have some causative factor in common.

*Blood Changes.*—Red cells little diminished at first, become less numerous as disease advances, but relatively not very pro-

nounced anemia; cells may be undersized; nucleated forms uncommon. Hb always diminished. Leucocytes normal or diminished, with a tendency to lymphocytosis; but there may be leucocytosis up to 50,000--60,000.

**Anemia Infantum, von Jaksch's Anemia.**—This occurs in infancy and resembles leukemia without the visceral lesions. The red cells are diminished, nucleated forms numerous, leucocytes generally increased. The spleen is enlarged with hyperplasia of its elements. The liver may be large and the lymph nodes also.

**The Blood in Fevers.**—The red cells are diminished in number, partly due to destructive effect of high temperature, coagulability diminished or increased, albumins diminished; hydremia and decreased alkalinity claimed by some observers and denied by others. The blood may contain the organisms of the disease in question.

**Hemophilia** is an inherited abnormality of the blood or the vessels of both, which leads to severe spontaneous hemorrhages or great and uncontrollable bleeding after very slight wounds (extraction of teeth). The condition passes from males to males through females who are not affected. Thinness of the arterial coats and narrow caliber, disproportion between the total blood and the capacity of the vessels, local vascular hypoplasia, and obscure nervous conditions, have all been supposed of importance in etiology. The blood takes longer to clot than normally, but may not be deficient in fibrin. No constant alterations in the cells or the composition of the blood have been demonstrated.

**Purpura Hemorrhagica, Morbus Maculosus, Werlhoff's Disease.**—This is a disease of unknown etiology, though it appears as if certain cases were connected with the presence of bacteria, pyogenic chiefly. It is characterized by bleedings into and from skin, mucous and serous surfaces, by high temperature in some cases, no temperature in others, and usually a rapidly fatal course. The blood clots slowly and imperfectly,

leucocytosis is present at times, blood plates are at times scanty. Non-febrile cases sometimes resemble pernicious anemia in their blood characters, but differ from it by absence of megaloblastic changes in blood and marrow and by the clinical symptoms of marked hemorrhage. From the febrile form they differ in presenting less leucocytosis, more hemorrhage and no infection symptoms. The red cells are much reduced in number, small, nucleated forms rare; leucocytes normal or reduced, with large per cent. of lymphocytes.

**Scorbutus; Scurvy.**—Beyond the association with imperfect and improper diet the cause is unknown. Anemia, ulcerating gums and loss of teeth, bleeding in skin, mucous and serous membranes, general fatty degeneration of viscera, enlarged spleen, edema and hemorrhage in joints, may occur together or with certain features omitted or increased. The blood shows decrease of red cells corresponding to the hemorrhage, pale and broken cells and microcytes may be present; Hb is decreased; leucocytosis relative or absent.

**Parasites.**—The chief forms occurring in the blood are the bacterial, in septic diseases and relapsing fever, and in these only at short and uncertain intervals; the organisms of malaria, variola, and yellow fever, which complete their human cycles in the fluid, the spirochete of relapsing fever, and the filaria sanguinis hominis, which occurs chiefly at night and after rest in bed. (See Part I., Chaps. VIII. and IX.)

# CHAPTER XIV.

## THE RESPIRATORY SYSTEM.

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### The Nose and Adjacent Cavities.

**Malformation.**— Various degrees are encountered in the nose, from complete absence with one-eyed infants (cyclops) to good external formation but lack of the septum or one or more turbinate bones, deviation of the septum and closure of one or both nostrils by bony growths, or by folds of mucous membrane. The extreme cases occur in non-viable infants; the less marked are amenable to surgical care.

**Circulatory Disorders** are common in the nose, the rich supply of blood-vessels in parts of its cavity disposing the mucous membrane to sudden hyperemia and inflammation; more chronic congestion leads to various hypertrophies. In either form of congestion hemorrhage is common, giving all degrees of epistaxis. Such bleeding from the nose is observed in typhoid fever, purpura, hemophilia, pernicious anemia and diphtheria. Usually its source is rupture of a vein, caused by external violence, blows, efforts at clearing the passages, and if excessive and repeated the hemorrhage may be the beginning of profound anemia or even fatal. The blood usually appears externally, or is partly caught in the mouth; if patients are weak or asleep the blood may be drawn into the larynx or aspirated into the lungs. More often it is swallowed.

**Inflammation** of the nasal mucosa occurs as an acute catarrh from various simple causes, direct and reflex. There is a stage of active hyperemia and dryness, followed by free outpouring of altered discharge which may excoriate parts it

bathes, as the lip and nostrils. This contains mucin and white cells with countless bacteria at first, but in later stages may become purulent and epithelia are found. Attacks of this nature frequently repeated are apt to end in chronic rhinitis and extend to the posterior pharyngeal wall. Streptococci and staphylococci, diplococcus pneumoniæ and other forms are almost constant in the healthy nose, and it is probable that when the conditions favor they may set up the inflammation; just as the colon bacillus, usually a harmless inmate of the intestine, may cause severe suppuration when the normal resistance of the intestinal wall is lessened.

Nasal hyperemia and inflammation may be due to vaso-motor disturbance in the territory of the trigeminus, and such conditions show a marked annual periodicity in some persons, occuring regularly every summer as certain plants ripen and scatter their pollen. Among these the ordinary ragweed (ambrosia) has very irritating pollen.

*Chronic rhinitis* may simply follow the acute form, but is often connected with depressed states of the system. It is characterized by stasis in the numerous veins, hypertrophy of the membrane and increase in the size of the glands; it is usually localized about the lower turbinated bones and adjacent septum, but may be general. After a course of years the newly formed fibrous tissue shrinks and an atrophic stage begins, with destruction of glands, retention cysts of their ducts, thickening of the vessels and decrease in their lumina. The most severe grade of such a process appears in *rhinitis atrophica fetida,* ozena, as commonly encountered in syphilitic and tubercular children. The altered and partly purulent secretion combining with the ulceration of the cartilages and turbinated bones produces an extremely disagreeable odor. The septum may be lost and the bridge of the nose obliterated, so that the nostrils look straight forward. The bacteria found may be the usual pyogenic or the pneumonic cocci, or saprophytes which cause the decomposition of the altered excretion.

**Infectious Granulomata.**—*Syphilis* usually causes a coryza in the earlier stages which differs but little from any acute rhinitis. Later there may be superficial ulcers on the mucous membrane or perichondritis and periostitis of the bones about the nasal cavities, or gumma, which lead to necrosis of parts of the nasal walls and indolent ulcerations. Such ulcers are common on the septum and often perforate it. *Tuberculosis* is met with in several forms, as a general scrofulous rhinitis, or as localized polypoid growths and ulcers. Commonly it follows artificial inoculation by the use of handkerchiefs soiled with sputa, or from picking the nose, or lupus of the face may perforate into the nasal cavity, or the disease may appear there as a primary affection. The cervical lymph nodes are apt to become involved and caseous.

From the horse afflicted with glanders the bacillus mallei may pass to the human nasal membrane and cause nodules, "farcy buds," and ulcers to develop, and in both leprosy and rhinoscleroma the nose is apt to be involved sooner or later. Pp. 249 and 678.

**Tumors.**—The simplest and commonest nasal tumors are polypoid growths composed of fibrous tissue and myxomatous material in varying amounts, and when the latter element is very fluid the resulting tumor is a cyst. Papillomatous growths develop in the lower third of the nasal channel, as is the case also of fibromyxomata. Either of these may be combined with hyperplasia of the mucous membrane and glands, the latter usually widely dilated. Chrondroma, osteoma, sarcoma and other forms occur, the latter usually starting from the wall of one of the adjoining cavities (as the antrum), and pushing its way out and down. Carcinoma is less common, but epithelioma may develop about the nostrils, as so often where skin and mucous membrane become continuous.

In the various cavities of the skull which open into the nasal passages, the frontal, sphenoid and maxillary sinuses, similar affections of their bones and lining membrane occur as in the

nose, but often their clinical importance is greater because of their distance from the surface and the limited space which confines the accumulating products of disease.

## The Larynx.

**Malformations** of the larynx are not common or of great importance; the organ as a whole may be small in general aplasias connected with hypoplasia of the vascular system, cryptorchism, etc.; sundry parts may be lacking or unsymmetrical, as the epiglottis, or the sinus of Morgagni may be dilated to a large air-filled space (as in monkeys), or fistulous canals may communicate with the outside from imperfect closure of branchial clefts.

**Disturbances of Circulation** are frequent. Anemia may be part of a general anemia, and often is the first sign of laryngeal tuberculosis. Active congestion of various grades follows inhalation of irritant gases and dust, the fatigue of long (and improper) use, and is the first stage of acute inflammation. Passive congestion occurs in circulatory disturbances from disease of the heart and lungs. Hemorrhages may be punctiform and limited to the submucous tissue, and are found after extreme acute hyperemia, from choking, in scorbutus and hemophilia; massive bleeding follows ulceration which opens a vessel of importance. Edema is clinically of great moment, especially in the young, because of the limited space and the importance of its function. It is common with passive hyperemia and chronic inflammation, but may develop suddenly with fatal consequences from irritants, inhalation of steam and gas, and in the course of nephritis and other disease accompanied by edema. The laryngeal picture is that of two pyriform masses corresponding to the arytenoid cartilages and the aryepiglottic folds, which meet in the middle line and overhang the rima glottidis, closing off its posterior two-thirds at first and then the remainder; with each inspiratory effort these masses tend to be drawn downward and together shut off the supply of air completely.

**Inflammation.**—*Acute laryngitis* begins with hyperemia of the mucous membrane, increased secretion follows, and the voice becomes husky and aphonic from imperfect vibration of the thickened vocal cords.

Strictly speaking these are neither cords nor bands, but triangular prisms, one side applied to the wall of the larynx, their upper horizontal surfaces visible in the laryngeal mirror, their sloping lower sides unseen, their thin edges approaching in the middle line and capable of tension and approximation by the muscular apparatus of the larynx; being highly elastic they contract as the tension is lessened. They ought to be known as the vocal prisms, then, but long usage has sanctified the incorrect term "vocal cords."

The secretion is either increased mucus alone or contains leucocytes also; if its proportion of pus-corpuscles is high, the mucous membrane is usually very much swollen, and shallow ulcers form on the posterior commissure and the posterior surface of the epiglottis. When the follicles are involved in such ulceration the resulting loss of substance is much deeper and healing is followed by scar formation.

*Chronic laryngitis* may develop from the acute process, often after repeated attacks, or slowly and independently. Slight varicosities are noticeable in the mucous membrane, the secretion is scanty and thick, the mucous membrane is thickened and from its swollen glands may have a coarsely granular appearance. On the vocal cords little patches of thickened mucus cling and the usual glistening look is lost; small ulcers of mucous follicles are common. Such chronic laryngitis is often found in those who are obliged to talk long and loud (as auctioneers), in habitual drinkers and in those who suffer from pulmonary tuberculosis and other lung diseases. As elsewhere, an atrophic stage may follow the hypertrophic, and small papillary hypertrophies may occur and persist (verrucous laryngitis).

*Croupous Laryngitis.*—In exudative inflammation of the larynx, when the exudate contains fibrin and coagulates, with its

contained pus-cells it makes a false membrane of grayish color and fairly tough consistence which clothes part or the whole of the interior of the larynx. It may be disposed merely as delicate patches or form a complete cast of the cavity and at first it is closely connected with the mucosa; such a membrane may be coughed out and reproduced in a comparatively short time. Microscopically there are fine and coarser filaments of fibrin, which stain with the Weigert method, entangling desquamated epithelium and pus-cells, seldom a few red cells also; under it the epithelium is lost and the glands are dilated from retained secretion.

*Chondritis* and *perichondritis* of the laryngeal cartilages is commonly a secondary affection after ulceration in the larynx, most often tubercular and syphilitic. At first but one cartilage is affected, then the inflammation spreads to others, the nutrition of the part suffers and the non-vascular cartilage dies. The pus and tissue detritus may exert a strong pressure on the larynx and interfere with breathing, or it may point and discharge through the larynx or externally.

**Tumors.**—Commonest of all tumors in the larynx are the papillomata, which resemble similar tumors of the external skin. They may be broad and but little raised above the surface, or furnished with a pedicle and capable of rather free motion. They appear at any age but most often in adults, and are covered with flat or cylindrical epithelium or transitional forms. Mucous hyperplasia may result in the formation of polypoid tumors, on the edges of the cords or elsewhere, and the microscopic picture is that of fibroma. Mucous polyps differ in having enlarged and degenerated glands mixed with the fibrous tissue and, from the distention of these, the tumor may become cystic. True adenoma is not common, either here or in the nose. Malignant tumors may occur, though not very frequently as primary affections, and of these epithelioma is most common, starting from the vocal cords or from portions of the

larynx which are covered with pavement epithelium. Metastasis to adjacent lymph nodes and the lungs is common.

**Infectious Granulomata.**—*Tuberculosis* of the larynx is usually an infection by the tubercle bacillus upon a chronic laryngitis; less often it is primary. It appears as a single ulcer, frequently about the posterior commissure or the posterior aspect of the epiglottis, while the rest of the larynx is free, or several ulcers in these and other sites, at times almost destroying the free edge of the vocal cords. If the ulcerative process extends to the submucous tissues fatal edema may occur, or perichondritis and necrosis of the cartilages. Between the ulcers the mucous membrane may be hypertrophic or even verrucous. A peculiar and unusual form of laryngeal tuberculosis occurs by extension of lupus inward from the face.

*Syphilis* of the larynx, as in the nasal mucosa, varies from a simple catarrh to infiltration of both mucous and submucous tissues, deep ulceration and destruction of portions, as the epiglottis. When the ulcers heal, firm scars of large extent may narrow and distort the part.

*Leprosy* occurs in the larynx as nodules or less often as a diffuse infiltration. Glanders produces small nodules which break down and leave deep ulcers; the epiglottis seems especially liable to such lesions but they occur deeper in the larynx also. Occasionally rhinoscleroma of the larynx has been encountered, in the later stages of the disease.

**Foreign bodies** may be solid objects, food, coins, buttons, etc., held in the mouth and accidentally inspired, or pieces of food misdirected in swallowing, or rags and other matters introduced (in the new-born) with criminal intent. Blood, vomit, pus, etc., may also be inspired and close the orifice temporarily or fatally.

**Wounds.**—The commonest are self-inflicted from attempted suicide and while not immediately fatal, even though the pharynx be opened, yet blood or food may enter and cause asphyxia or discharges may be inspired and set up a pneumonia. To this

subcutaneous emphysema may be added. In hanging and choking the larynx may be injured from the squeezing, but usually it escapes by being lifted upward and backward into the oral cavity. In the aged, when the cartilages are calcified, breaks may occur more easily, and even the hyoid bone may be fractured; this is seldom the result of direct violence, more often it follows severe muscular exertion as in vomiting and is rare from any cause.

## Trachea and Bronchi.

**Malformation.**—The only anomaly of development of importance is the occasional appearance of a fistula due to the imperfect closure of the third or fourth branchial cleft. The fistula opens by a small orifice on the anterior edge of the sterno-mastoid, oftener on the right side, about 3-4 cm. above the inner end of the clavicle, and may communicate with the trachea or end blindly in the tissues. The inner portion is at times much dilated, and is then termed a branchiogenic cyst.

The trachea is seldom diseased by itself; usually it is inflamed when either the larynx or the bronchi are inflamed and in a manner similar to the main disease. Aneurysms and malignant tumors may break into the tube. Tumors are not so common as in the larynx and infectious granulomata are secondary to similar lesions in the lungs or larynx. All that may be true, then, of the pathology of both the upper and the lower portions of the respiratory tubes will be true of the trachea and does not require special description.

## Bronchi.

**Circulatory Disorders.**—The disorders of the larger bronchi present but little differences in their pathology from those of the trachea and larynx, but in the case of the smaller divisions of these tubes new factors enter which require special mention. The finer divisions are easily diminished in lumen when the

lining cells are swollen, they are easily obstructed by inflammatory exudates, and inflammation in their walls almost always passes over to the tissue of the lung; hence capillary bronchitis should be considered with diseases of the lung. The larger bronchi are usually anemic on post-mortem examination, for their elastic fibers press the blood out. Hyperemia may be acute and arterial from irritation by dust and other inspired matters, or very commonly it is passive and dependent upon cardiac disease, especially in lesions of the mitral valve. But a small portion of the blood from the bronchial wall returns by way of the cava and azygos veins, the larger part returns by the pulmonary; hence any uncompensated obstacle in the left side of the heart must produce chronic passive hyperemia. This appears post mortem as a dark red or even brownish discoloration of the mucous membrane, swelling of its layers and increase of its secretion, the bronchi being filled usually with muco-pus; owing to the presence of air the color may be bright red and simulate active hyperemia. Hemorrhage may occur from the presence of foreign bodies, or as the result of ulceration of any variety. When an aortic aneurysm opens into a large bronchus sudden and fatal hemorrhage occurs, but this is strictly not a bronchial bleeding; if the patient survives the immediate effects a fatal result may occur by pneumonia from the inspired blood. Similar loss of blood by way of the bronchi is relatively common in tubercular diseases of the lung and erosion of pulmonary vessels.

**Inflammation.**—*Acute bronchitis* may be primary or secondary to tracheitis. As in other mucous membranes, the first stage is an arterial hyperemia with swelling and lessened secretion; then follows a copious flow of thin mucus with but few cells, or of thicker and tougher sputum with more pus and a yellower tinge. Such an inflammation at the two extremes of life is more serious than in vigorous adults; the danger increases inversely with the size of the tubes involved and when the smallest divisions are inflamed (capillary bronchitis, bron-

chiolitis) the mortality is practically that of pneumonia. Abundant sputa may be termed *bronchial blennorhea* when very thin and *pyorrhea* when thick and purulent.

*Chronic bronchitis* follows acute attacks or develops in connection with chronic diseases of the lungs in which there are persistent circulatory and nutritive disturbances, as in emphysema and some forms of tuberculosis. The mucous membrane presents the same appearances as elsewhere, swollen and congested layers, papillary projections (villous bronchitis) and at times also the atrophic condition of glands, mucosa and muscular elements. The secretion may be light and viscid or profuse and more purulent, and where the bronchi are dilated such secretion may collect for a long time and undergo decomposition.

*Croupous Bronchitis.*—This form of acute bronchitis may be due to the inspiration of irritants, but most commonly it follows diphtheritic infection. With every croupous pneumonia, and with laryngeal croup which descends, there may be a similar affection of the bronchi. The first stages may be like an ordinary catarrhal inflammation or with extreme dyspnea, and high fever; after the lapse of a few hours or days the peculiar sputa appear. The inflammation may affect the entire bronchial tree and in this case is of very grave prognosis. In the chronic form the disease may follow an acute attack of any bronchitis or it may develop in connection with chronic lung diseases, and frequently it is limited to a certain section of the bronchial territory. Dyspnea is hence less marked in the chronic form. The characteristic sputum is of a yellowish-white color and when spread out in water reproduces the branching of the air passages; complete casts of large sections are not infrequent in the chronic form. Casts of the larger tubes may be hollow, those of the finer are solid, and sometimes made of concentric layers of coagulated material. This is often considered to be fibrin, but only the middle of a cylinder gives the fibrin reactions, while the rest is

evidently thickened mucus. Tangled in the meshes of the coagulum are many white blood cells and degenerated epithelia and frequently the peculiar crystals which are thrown off in asthma, and found also in prostatic secretion, called Charcot-Leyden crystals. These are slender double pyramids (octahedra), at times bent on the edge or the flat or spirally, transparent, supposed to be related to nucleo-phosphoric acid and derived from leucocytes in most cases; they measure about 40 $\mu$ by 6--8 $\mu$. Another element in the sputum is the Curschmann spiral, long twisted and slender coagula surrounded by a fringe of very delicate fibers.

*Diphtheritic bronchitis* occurs as a complication of the same disease in the pharynx and larynx and the pseudo-membrane presents the same characters as elsewhere, or, more commonly, the process is croupous in the bronchi and diphtheritic in the pharynx.

*Putrid or gangrenous bronchitis* may accompany gangrene of the lung, due to infection by particles of necrotic lung tissue. The mucous membrane is softened and destroyed and hangs in decomposed shreds from the wall.

*Peribronchitis* and inflammation of the entire wall of the tube occur frequently with tuberculosis of the lung.

**Stenosis and Dilatation.**—The lumen of a bronchus may be narrowed by inflammatory and other swelling of the lining membrane and by pressure from without, tumors, cicatricial tissue, etc. The area of lung supplied may collapse (*atelectasis*) or become inflamed, or, if a little air can enter but escapes with difficulty, the lung tissue may be emphysematous. Foreign bodies also close the bronchial lumen more or less completely, with ulceration from pressure where they lodge, inflammation of the lung, perhaps gangrene; usually they lie in the right bronchus.

*Bronchial dilatation* (bronchiectasia) may be limited to but one or a few branches or distributed over large sections; the middle sized branches are oftenest involved and at the same

time the finer divisions beyond may be obliterated. The dilatation may be sacculated, fusiform, cylindrical or irregular, and in the wall of the dilated portion nearly all the elements are atrophied; the mucous membrane may be swollen or thinned and its secretion is abundant and purulent or nearly absent. Fibrous thickenings about the dilated bronchus lend its walls an apparently normal size. When many of the bronchi are in this condition the lung tissue between presents degrees of compression, with irregular communicating passages through it, and this condition has been called *bronchiectatic phthisis.* Collections of mucus and pus may decompose and set up gangrene, or undergo drying and calcification. All forms of dilatation are usually associated with chronic bronchitis and lessened resistance in the bronchial walls. This is especially marked where the lung tissue is the seat of fibrous hyperplasia, for then the inspired air exerts a pressure upon the weakened wall of the tube and the fibrous tissue, contracting from outside, assists the dilating action.

**Tumors.**—In the bronchi primary neoplasms are very rare, while secondary are common from the ease with which the returning blood current may carry particles from distant tumors to the vessels of the lung. Carcinoma may develop from the muciparous glands of the bronchial mucous membrane, usually of a middle sized tube and in the lower lobes.

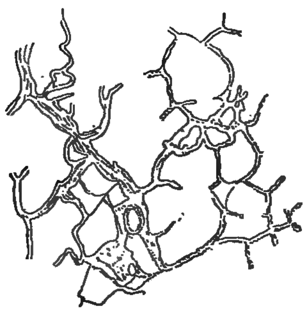
**Infectious Granulomata.**—Both tubercles and syphilitic scars are found in the bronchi, the former is an almost constant lesion in various forms of tuberculosis of the lung. A few or many shallow ulcers in the mucous membrane are found, some of which may pierce even to the cartilage or the outer layer.

## Lungs.

**Atelectasis.**—In consequence of debility the new-born infant may be unable to draw air into the lung and it remains in the fetal condition; injuries to the brain and cord during parturition

and foreign bodies, as mucus and amniotic fluid, in the upper air passages produce the same result. Only part of one or both lungs may be atelectatic and appear solid, small by comparison, bluish or brownish red, not crepitating, non-elastic. If the atelectasis is recent the portion involved may be blown up by forcing air in and resembles normal lung. In the adult, parts which have become atelectatic may be solid and tough, anemic, pigmented or not, compressed by fluid, adherent by the pleura to the side of the thorax, or presenting a bronchus whose lumen is obliterated at some point. The bronchi show hypertrophied

FIG. 88.



EMPHYSEMA OF THE LUNG; LOW POWER. DILATED VESICLES WITH RUPTURED AND NON-VASCULAR WALLS.

mucous membrane with villi and swollen glands and the cartilages may be relatively or actually hyperplastic. Any lung or part of a lung deprived of its air will sink when thrown into water. The fate of a non-aërated part is either inflammation or fibrosis and calcification.

**Emphysema.**—When an air passage is opened by a wound and the air from it gains entrance to the interlobular tissue of the lung, sometimes also after ulcerations, the condition is called *interstitial emphysema* and resembles a similar state of the subcutaneous cellular tissue. The lung appears pale and dis-

tended and under the pleura are small collections of air which may be pushed about by gentle pressure. Rapid decomposition produces the same appearance at times, the gas collecting under the pleura.

*Vesicular* or *substantial emphysema* is the name given to permanent dilatation of the vesicles and is a chronic disease with important secondary results. The dilatation may be due to loss of resisting power in the lung tissue, closely associated with imperfectly developed elastic tissue, and to continued and violent expiratory efforts. An *inspiratory emphysema* has been described as occasioned by a partial vacuum in the chest, when the smaller bronchi are closed by swelling of the mucous membrane and the expansion of the thorax is unable to fill the alveoli. *Compensatory* or *vicarious emphysema* occurs when one portion of the lung is functionally incompetent and the rest exposed to greater air pressure because of dyspnea; it is common in the unaffected lung when the other is the seat of lobar pneumonia, or when adhesions and congenital atelectasis lessen the volume of a lobe. This vicarious condition appears especially on the edges of the lungs and close inspection discovers widely dilated alveoli under the pleura; where many of these coalesce it is termed *bullous emphysema*. The portions of lung which make the largest excursion during the respiratory act are the most often dilated and the condition is found in both acute and chronic lung affections.

Two elements enter into the explanation of the gravity of true or alveolar or vesicular emphysema. The first is that, despite the apparently larger volume of the lung, the actual breathing surface is much decreased, because the dilated alveolar walls become thinner and thinner and gradually disappear; and secondly, in proportion to the extent of the former change, the number of permeable capillaries, and the total blood content of the lung, diminish. Such lungs on autopsy fill the thorax and do not collapse when it is opened, the ribs and sternum are in the position of full inspiration and the diaphragm is as low as

the seventh rib, the lungs cover the heart and look pale and dry. The anterior sharp margin is rounded like the posterior, the entire lung is yielding and non-elastic, and the dilated alveoli and groups of alveoli are clearly apparent on gross inspection. With this condition nearly all the elements of the lung structure are atrophic, even the large vessels and the walls of the bronchi; with the latter there are frequent dilatations. Commonly also a chronic bronchitis is evident from the thick muco-purulent secretion in the tubes. As a general result of the imperfect use of inspired oxygen and lessened blood content of the lung, the condition of the patient suffers severely. To this are added the effects of the mechanical obstacle to the venous current, such as dilatation of the hepatic vein and its radicles, imperfect liver function, edema of the feet and legs, dusky hue of the surface generally, cardiac hypertrophy and dilatation (right side) and serous exudates in various body cavities.

A form of emphysema in the aged is due to simple atrophy and diminished nutrition in the lung and the organ is decreased in volume.

**Circulatory Disorders.**—The double circulation through the lung is important to remember in this connection, the capillaries derived from the pulmonary artery subserving the function of the organ, respiration, while its nutrition depends upon the bronchial artery, which supplies the walls of these channels and also the visceral pleura; anastomoses between the two are unimportant in normal conditions.

*Pulmonary anemia* may be part of a general anemia or may follow pressure from pleural exudate, tumor, etc., and atrophy of the capillaries as in emphysema. In the adult, especially the dweller in cities, the color of the anemic lung is gray because of the foreign pigment; in the infant it may be pink.

*Hyperemia.*—A form of congestion of the lungs affecting dependent portions is common in the cadaver and is known as *hypostatic congestion;* this usually is found in the posterior, *i. e.,* inferior, portions of both lungs when the body lies on its

back It is quite possible that a lung which was actively hyperemic during life should show the condition only in dependent portions after death, so that hypostatic congestion is not always without clinical significance.

*Acute hyperemia* of the lung follows excessive muscular effort, especially if protracted, and may lead to edema of the organ; cardiac dilatation is an important factor in this result. It is caused also by an irritant which may be inhaled, and collateral congestion may follow sudden cooling of the body surface and lessened blood content of one lung by compression. It is the first stage of inflammation of the organ, or pneumonia, and is specially marked in the lobar form; such a congestion differs from simple hyperemia in that the lung is already friable.

*Passive congestion* usually follows chronic disease of the heart, especially mitral lesions and myocardiac degenerations; it is also observed with chronic bronchial inflammation. In marked degrees of such chronic congestion the lung takes on a peculiar color and becomes firm in consistence. In the alveoli and the septa are found granules and masses of pigment, at times free, at times enclosed in leucocytes, which are the remains of red cells which have wandered out of the overfull capillaries. To this condition the name of *brown induration* is given, or, as the interalveolar septa are usually thickened, it has been considered as a low grade of productive inflammation and termed the *pneumonia of heart disease*. In the sputa of such a case leucocytes bearing pigment often occur.

*Hemorrhage.*—On autopsy the evidences of bleeding in the lung vary from small punctiform hemorrhages which require careful search, to filling and partial destruction of a large section of the organ (lung apoplexy). The blood lies in the tissue of the lung, between the alveoli as well as in them, when it comes from the organ itself. When the source of the bleeding is external, as from operation about the upper air passages, the bronchi contain most of the blood, but little may be found in

the alveoli; small amounts inspired may reach the alveoli. The seat of such collections is often in the lower portions of the lung, on one or both sides, where scattered dark red masses appear, corresponding to one or more lobules, the central portions deeper in color than the periphery. Hemorrhage may result from injury, as puncture by broken ribs, and also after cerebral apoplexy from vaso-motor spasm.

*Infarcts* may be one or many, usually sharply defined from the rest of the tissue, prominent and superficial, lying under the pleura and often along the edge of a lobe, of a deep red color and firm to the touch. They are compared to a cone or wedge in shape, the apex in the tissue and the base external, but many other and irregular forms are found. The alveoli are stuffed with red blood cells and the septa show the effects of pressure, hyaline and fatty degeneration. The infarct may arise from embolism or thrombosis of a pulmonary vessel or in the course of chronic venous stasis. About the infarct there is usually a zone of inflammation, and if the embolus contains microörganisms, or they gain entrance from the air, suppuration and gangrene of the part may follow. In other cases the blood is partly absorbed, partly converted into pigment and the injury healed by new fibrous tissue which contracts later.

An occasional result of large *emboli,* usually coming from the posterior crural or femoral veins or the inferior vena cava, is sudden death. The lungs are pale, distended by the severe dyspnea which accompanies the case, and behind the embolus, in the pulmonary artery and the right heart, there is an excess of venous blood.

*Fat embolism* is observed in the pulmonary capillaries after fracture of large bones and destruction of the marrow, also in severe injuries to adipose tissue, as burns and bruises. The fat appears in droplets and larger masses, liquid but caught in the capillaries, or even in large branches of the pulmonary artery. If the total amount of fat interferes with respiration it may produce death from pulmonary edema; smaller amounts may be

pushed forward and lost in the arterial circulation, or may reproduce the embolism elsewhere, as in the brain.

*Edema.*—When there is a sudden outflow of serum into the tissue of the lung and the alveoli it is known as *pulmonary edema* and it may be acute and immediately fatal, or more slowly developed and less marked. The lung is paler than usual, unless at the same time congested, it feels firm, parts of it even resembling hepatized lung, and on section a frothy fluid escapes in quantity; both lungs or a part of one may be involved. With inflammation of part of a lung the rest is apt to become edematous. Pulmonary edema occurs as the final stage of heart and kidney disease and occasionally in alcoholic and insane patients. The cause of edema of the lung is frequently a loss of power in the left ventricle while the right continues to functionate, the extreme degree of stasis attained leading to rapid transudation. On dropping a piece of such lung into boiling water for half a minute the albuminous serum coagulates and may then be demonstrated between the alveoli as well as in them.

**Gangrene.**—After a portion of the lung has undergone necrosis (as coagulation) the access of saprophytic germs may set up putrefactive changes exactly similar to those which occur in the air in any dead tissue. Aspiration of decomposed tissue and pus from abscesses, perforation from the esophagus, cancerous or otherwise, and foreign bodies in the bronchi may be exciting causes of gangrene. Emboli from distant parts also produce pulmonary gangrene, and cancer and rarely tuberculosis may terminate in it. Alcoholic habits seem to predispose to pulmonary gangrene. Two forms of the lesion are recognized, the *diffuse* and the *circumscribed.* The latter appears as spheroid or ovoid foci, often multiple, of a black or green color and foul odor, surrounded by a zone of edematous and congested or inflamed tissue. A line of demarcation forms, the decayed tissue softens and separates from the rest, and may be expectorated or persist as a thick broth of broken-down

putrefied tissue. Through such a cavity a bronchus or a vessel may still pass, though the first shows inflammatory reäction or necrosis of its walls and the latter is filled with a thrombus; if the vessel is opened severe bleeding may occur. Should the edematous and inflamed tissues about such a focus take part in the gangrene the process spreads and we have the diffuse form which is rapidly fatal. Such gangrene is of the moist variety on account of the rich supply of blood in the organ. It may pass over from the lung to neighboring parts, break into the pleura or pericardium, or cause emphysema of the skin of the thorax after adhesion and perforation of the two layers of the pleura. If the patient survives long enough septicemia appears and there may be embolism of distant parts and secondary gangrene. Although the prognosis is grave, yet a gangrenous process may be healed, after evacuation of the softened material and suppuration and granulation of the cavity.

Putrid bronchitis is a regular accompaniment of gangrene of the lung and the characteristic sputa, red or even purple, thin and foul, with an offensively sweet flavor, are pathognomonic. In a glass the sputa settle in three layers, the top foamy, grayish or yellow, the middle transparent and thin, the lowest reddish-brown or purulent or mixed with particles of lung tissue. In the sediment the microscope discovers triple phosphate crystals, needles of margaric acid, fat in drops and granules, elastic fibers, pus cells and pigment. The organisms may be staphylococcus aureus and albus, filamentous and branched forms (streptothrix), and ciliated monads.

**Pneumoconiosis.**—Workers in dust of many kinds are liable to inspire finely divided particles of inorganic matter. If coal dust is the chief element the condition is called *anthracosis;* iron and steel particles cause *siderosis;* workers in stone inspire quartz and other dust (*chalicosis*); millers and bakers inhale flour (*farinosis*). For a time the lung is very tolerant of such foreign material, and it is laid away in the interlobular connective tissue and the bronchial lymph nodes without apparent

damage to the function of the organ. But beside the mechanical irritation, to which the response is commonly a fibrosis of slow development, the foreign particles may not be aseptic, or they may make microscopic wounds of the mucous membrane, and in either case more violent inflammation may follow. Mild degrees of bronchitis are frequent and the foreign matter is in great part expectorated with the secretion. In the alveoli a desquamative process goes on and the epithelia may degenerate and also be coughed out; cells containing pigment are usual in such sputa. Occasionally the dust passes into the general circulation and is excreted in part by the liver and in part by the intestinal mucous membrane. After a time a form of lobular pneumonia may develop, or the already weakened lung is infected with the bacilli of lobar pneumonia or tuberculosis.

Milder degrees of such dust inhalation are the usual thing in post-mortem findings; on the pleural surface there may be multiple miliary fibromata, in the lymph nodes the tissue is uniformly black, and through the lung in all fibrous parts similar pigment is found. The contrast between the lung of the city dweller and that of the person always residing in the country, is very marked; in the infant the lung is bright red or pink and entirely free from foreign pigment.

**Wounds and Foreign Bodies.**—When foreign bodies enter by the bronchi they are apt to set up an inflammation which involves the lung tissue secondarily, and this may end in gangrene. Entering the lung otherwise they imply a wound, and bullets, pieces of broken rib, or clothing, driven in by violence are probably commonest. Other wounds of the lung may result from severe compression and contusion of the thorax, stabs, etc. If of small extent and closed by pleural adhesions these may heal. Another variety of wound occurs from rupture of abscesses in the lung or adjacent viscera, as the liver, when the weakened lung tissue may be torn by respiratory and other muscular efforts.

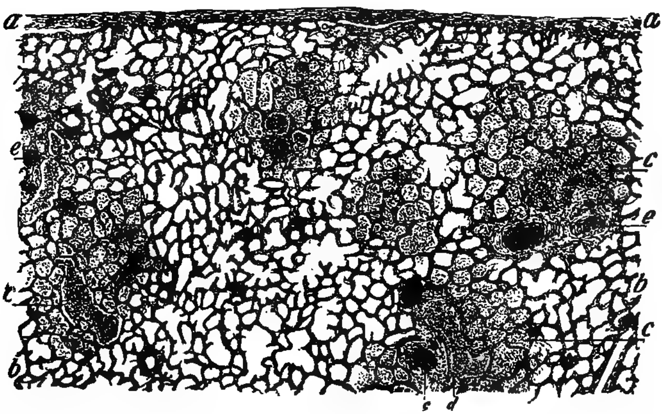
**Inflammation.**—While *pneumonia* or *pneumonitis* is the name given to inflammation of the lungs, yet the disease occurs in so many different forms that it is necessary to classify them according to their anatomical or pathological characters. Thus from the nature of the inflammatory product we have *fibrinous* or *croupous, catarrhal, fibrous, purulent, caseous,* and from the part of the part of the lung involved we have *lobar, lobular, interstitial.* According to the path by which the irritant reaches the lung there are *broncho-, hemato-, pleuro-* and *lymphogenic* pneumonias, and when a visible excess of foreign material enters the bronchi it is called *inspiration pneumonia.* Lastly, in the cachectic, blood settles toward the dependent parts of the lung and a *hypostatic pneumonia* arises. According to the clinical course of the disease we have acute and chronic forms, and from special bacteria tubercular and syphilitic inflammations proceed.

*Lobular Pneumonia.*—In children especially, bronchitis of the finer tubes passes over to the lung tissue and causes pneumonia; this is a common sequel to pertussis, measles, and other infectious diseases. In the adult it follows typhoid fever and is associated with some forms of tuberculosis; in old age it develops from chronic bronchitis. Lastly, when matters of a septic nature are inspired they usually set up an inflammation of the same character, and it is possible for a patient with lobar pneumonia in one lung to inspire sputa into the other and thus present both lobar and lobular forms. The distribution of the disease in all these cases begins in single lobules and the air passages closely connected with them, the remaining lung tissue between being still supplied with air and capable of functionating. The affected lobules present in the alveoli serum, desquamated epithelia, red and white cells and mucus, the septa are infiltrated with round cells; the lobule is of a deep red color, prominent above the cut section, firm and friable, smooth on section, and non-aërated.

After a time the exudate undergoes granular and fatty de-

generation and the part becomes yellowish or gray. Normal tissue between may be blown up at autopsy by way of the bronchi, but the bronchi of the inflamed parts are closed by swelling of the mucous lining, or if still patent air does not reach the alveoli. The disease may begin in parts which have become atelectatic from closure of the bronchi. Developed from catarrhal pneumonia and often associated with it, one or both,

FIG. 89.




LOBULAR (ASPIRATION) PNEUMONIA. (*Ziegler.*)

*a*, pleura; *b*, normal lung; *c*, inflamed area; *d*, longitudinal section of a bronchiole; *e*, transverse section of an arteriole.

we may have a purulent and a hemorrhagic form. The suppuration begins in the alveoli which are filled with exudate and is due to the entrance of pyogenic bacteria; the infiltration about the alveolus is more marked than in the simple form, the exudate becomes fluid and escapes or remains as an abscess. Large numbers of red cells in the exudate give rise to the other form; from either, gangrene may develop. If the pneumonia become chronic the alveolar contents may undergo caseous

alteration, due to the presence of tubercle bacilli, and there is then marked fibrous proliferation about the bronchi and alveoli affected. The bacilli of influenza, anthrax and glanders frequently produce lobular pneumonia, and hypostatic and aspiration cases are usually of the same variety. Experimentally section of the pneumogastric nerve causes the same form. No one bacterium is exclusively the causative agent; many kinds have been recovered from these lungs, cocci, and bacilli, but perhaps most commonly it is the streptococcus which is most active.

*Lobar Pneumonia.*—In this form an entire lobe or the major part of it is uniformly involved, and there are no distinctions between alveoli which are filled with exudate and others which remain free scattered through the same part. In lobar pneumonia four well-marked stages may be distinguished — congestion, red hepatization and gray hepatization, followed by a stage of resolution.

*Stage of Congestion.*—The lung is intensely hyperemic, increased in size and firmness, abnormally friable, and contains little or no air. Under the microscope the capillaries about the alveoli are filled to the utmost with blood, and within the alveoli there is forming a very delicate reticulum of fibrin, holding swollen epithelia and white cells in its spaces.

*Stage of Red Hepatization.*—The fibrin is more copidus, the epithelia are almost wholly desquamated from the alveolar wall, and mingled with the exudate are numerous red and white cells. This exudate forms in each alveolus a tight plug, and puts the elastic fibers on the stretch. As soon as a cut is made in the lung these fibrinous plugs are forced a little way out of the alveoli and may be scraped off with the knife; the result is to give the section a peculiarly granular appearance. The part now contains no air and a small piece sinks at once when put into water. The total distention of all the alveoli makes the part as large as in full inspiration, and also very much firmer and heavier than in normal conditions. Other parts of the lung

are the seat of congestion, edema and vicarious emphysema. This stage marks the height of the disease.

*Stage of Gray Hepatization.*—With the beginning of regressive changes in the exudate the color turns from red to gray or yellow. The red cells in the exudate have lost their color, the pressure from within the alveoli makes it impossible for the blood to enter the capillaries, although they are not obliterated, and the entire mass has begun granular and fatty degeneration These changes gradually lead to the gray or yellow color which gives the stage its name, and as the inflammatory process advances it is possible to have all three stages present at the same time, the older parts being more nearly gray or yellowish-white in color. In alcoholic patients hemorrhages are frequent in the hepatized tissue, and here the red color persists.

As degeneration proceeds the contents of the alveoli become fluid and are either expectorated or absorbed by the lymph-vessels. Of the three lymph-systems in the lungs, one opens by at least one branch into the lumen of each alveolus and there are also foramina between alveoli. Should a lymphangitis accompany the pneumonia, as is very common, and the vessels become stopped, resolution proceeds very slowly, since removal by absorption is greater than by expectoration. The complete disappearance of the exudate in favorable cases takes comparatively little time and the lung returns to a practically normal condition; but often the elastic tissue has suffered with the rest and the alveolus recovers its elasticity slowly and imperfectly.

Croupous pneumonia may become purulent, either generally or in localized areas, but this is not common. An abscess formed in this way may break and discharge through the bronchi, or into the pleura, causing empyema; or if single and small it may become encapsuled and calcified. At autopsy careless handling of the friable hepatized lung may produce artefacts which closely resemble abscesses. In great constitutional depression, as cachexia, diabetes, senility, croupous pneumonia

may end in gangrene. If the part of the lung involved lies directly under the pleura it also becomes the seat of a fibrinous inflammation; this may leave adhesions between the lobes. In the apices of the lung croupous pneumonia is apt to resolve imperfectly and here tuberculosis frequently is the sequel.

Croupous pneumonia is usually lobar, but it may occur as a lobular inflammation after influenza. The disease affects the right lung, and the lower lobes, in men, more than the contrary of these. Associated with such affections of the lungs there is usually congestion and swelling of the spleen, cloudy swelling or acute inflammation of the kidney, and at times meningitis, especially in children.

The bacterial form most often encountered in pneumonic lungs is the diplococcus pneumoniæ of Fränkel, in other cases the bacillus pneumoniæ of Friedländer, in others colon bacillus, pyogenic cocci, etc. Before these bacteria can cause an inflammation of the lung, there must be an irritant or some other factor present which reduces the local and general powers of resistance; inspiration of air at too low a temperature, vasomotor reflex from the skin, and local or general disease are the commonest. The diplococcus pneumoniæ in other parts of the body may be pyogenic, as in meningitis, and as the exudate in the alveoli becomes more cellular after the fibrin coagulation is completed, the termination of the process in suppuration is easily explained.

A fatal termination of lobar pneumonia may be due to the extent of lung involved and loss of the respiratory function, and yet apparently complete double lobar pneumonia cases do at times recover; in other cases a toxic influence is more pronounced; or the heart may be overburdened, or the other lung may suddenly develop fatal edema; or gangrene and abscess formation end the case.

*Interstitial Pneumonia.*—The acute form may accompany either catarrhal or croupous processes, more often the former, and on the other hand a severe form may develop first and the

alveolar exudate follow. This is not common but it may occur in septic conditions of the system, or follow suppurative processes in the neighborhood; as when a gastric ulcer perforates the diaphragm and attacks the adherent lung. Another variety follows septic embolism, but here the suppurative inflammation is confined to one main vessel and its distribution. If rapid in their course the first presents as fine and coarser lines of suppuration in a large meshed network all through the lung, the latter as a group of small abscesses or a single large one.

The chronic form of interstitial inflammation consists in the steady proliferation of new connective tissue along the course of bronchi and vessels and between the lobules and alveoli. Rarely it is the sequel to acute pneumonia of either form, or it results from the irritation of inspired dust, or appears as an essential element in the chronic changes of tuberculosis and syphilis. In the bands of new tissue pigment deposits are common, and, as they contract, the total pigment is contained in less space and the color of the lung deepens as its consistence becomes firmer.

**Tumors.**—Primary tumors are not common in the lungs. Of the benign varieties lipoma, fibroma and chondroma have been described. In leukemia there are often multiple miliary tumors in the lungs composed of small round cells in a reticular stroma; they resemble tubercle but do not become caseous and they are both whiter and softer. Sarcoma is rare; it may be of the small round-celled variety or spindle-celled, and probably has its origin in the peribronchial lymphatic tissue. Primary carcinoma may develop from the crypts of the mucous follicles in the bronchi, and epithelioma has been described beginning in the epithelium of the alveoli.

Secondary malignant tumors are commoner, emboli from any organ reaching the lung and setting up tumors similar to the primary. Endothelioma may pass from the serous investment to the lung or begin in the lymph spaces of the organ itself. A form of carcinoma depends upon aspiration of fragments of

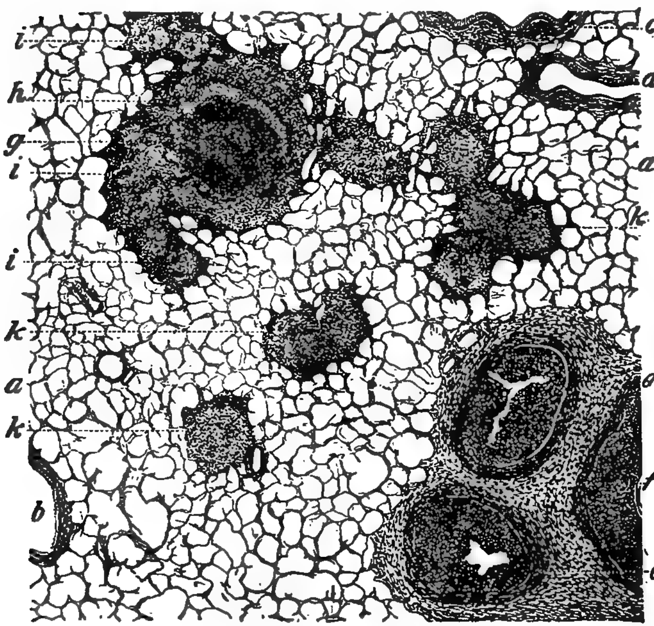
a malignant tumor situated in the upper air passages; they may be multiple and the largest, and presumably the oldest, may be cystic.

**Infectious Granulomata**. *Tuberculosis.*—Infection of the lungs by the tubercle bacillus may occur in three ways: through the bronchi, the blood-vessels or the lymph channels, termed *bronchogenic, hematogenic* and *lymphogenic* infection. However caused, the tuberculosis is a productive lesion, not an exudative. Tubercles may be found in any portion of the lung. In the connective-tissue elements of the organ tubercles resemble the same granuloma in any such tissue, made up of small lymphoid cells, large epithelioid and occasional giant cells. In the alveolar parenchyma they present peculiarities, being irregular and elongated in outline corresponding to the boundaries of the alveolus. The septa are thickened by round-cell infiltration, the alveolar lumen is reduced and its epithelial cells crowded together, leaving but a trace of the original space between. At other times the epithelia multiply, show mitotic figures, and fill the lumen till the boundaries between tubercle and epithelial tissue disappear; in such a mass giant cells often lie along what was the boundary of the alveolus. Lymphoid cells and pigment granules are also present. The giant cells are due to agglutination and fusion of endothelia, the epithelioid cells come from fixed connective tissue cells, and the lymphocytes are part of a reparative process. Tubercular granulation tissue, thus constructed, differs from inflammatory granulation tissue in containing no polynuclear leucocytes, and in being non-vascular, and hence doomed to destruction.

In the tubercle so established the usual degenerative changes occur — necrotic, hyaline and caseous — starting at the central portion, where nutrition is lowest, and spreading to the periphery; fibroblasts surround the focus and invest it with a capsule. The vessels of the part are obliterated and not even permeable for injection masses.

Bacilli are found in such tubercle both in the cells, giant and epithelial, and between them, but it is often hard to stain them. Pyogenic cocci may not yet have reached the focus, and until they do there is no suppuration, no softening of the tubercle

FIG. 90.




PRIMARY TUBERCULAR FOCI IN THE LUNG. (*Ziegler.*)

*a*, normal lung; *b*, normal bronchus; *c*, bronchus with inflammatory infiltration; *d*, artery; *e*, caseous mass with fibrous capsule; *f*, fibrous hyperplasia; *g*, caseous center, and *h*, cellular periphery of a tubercle; *i*, *k*, resorption tubercles, invading lymphatics.

and ulceration of the lung tissue, and clinically but little disturbance in the general condition, emaciation, fever, or night sweats. In other words, many of the symptoms which are always associated with tuberculosis of the lungs are due to a

mixed affection, the pyogenic bacteria attacking a tissue already weakened by the tubercle bacillus and rapidly destroying it. The tubercle bacillus is not cytotatic for polynuclear leucocytes.

*Miliary Tuberculosis of the Lung.*—As suggested above, the mode of entrance of the bacillus determines to a great extent the gross and microscopic characters of the disease. Tubercle granulations are most definite and typical when the infection enters by way of the blood current, hematogenic or disseminated miliary tuberculosis. The term miliary tubercle refers only to the size of the granuloma and the older yellow tubercles do not differ essentially from the recent gray translucent forms.

A lung affected in this way presents small firm granules of a more or less transparent look scattered through lung tissue which is not apparently much affected, and the lesion may be totally or partially disseminated. If rapidly disseminated through the whole of both lungs it is usually only a part of a general tuberculosis, and other organs — spleen, kidneys, meninges and choroid — also present tubercles; in this case the tubercle may appeal to the sense of touch more than to sight, requiring a side illumination and careful search. More slowly developed, chronic disseminated miliary tuberculosis may come from some focus elsewhere which allows a few bacilli to enter the venous current at intervals; as when a mesenteric or postperitoneal lymph node is attacked and bacilli make their way into the thoracic duct; here some of the tubercles are older and may show caseous changes. The lungs are still capable of functionating and between the tubercles may appear nearly normal; or lobar and lobular pneumonia may complicate the lesion, or simple hyperemia and edema.

When the entire lung is involved, as a rule the older tubercles, caseous and grouped, often surrounded by zones of caseous pneumonia, will be found in the upper lobes. Entering by the blood-vessels, the main distribution is along their course, and in the larger veins tubercles may be discovered in the wall on gross inspection; these may invade only the intima, and this

fact makes the mode of entrance clear. The name embolic tuberculosis has been given to the condition without good cause. The source of such a bacillemia may be found in some of the abdominal or systemic veins or lymph nodes.

Localized dissemination depends upon invasion of a vessel in the lung itself, so that only the territory supplied by it contains the tubercles. Thus a caseous bronchial gland or a tubercular process at the root of the lung may be the source of sudden dissemination through a lobe of one or the other lung. In other cases a tubercular mass as a center has distributed bacilli in a dwindling zone about it through the lymph channels, and such a distribution may occur as the result of invasion from a tubercular pleurisy; this process resembles metastasis of malignant tumors.

When tubercle bacilli are inspired they are disseminated through the finer bronchi and their favorite place for settling is just where the bronchiole ends and the alveolar passages begin. Here the bacilli become attached and set up a bronchiolitis, or inflammation already present may offer favorable conditions for development. Dust particles, especially with sharp edges, as fragments of iron, make microscopic wounds about which inflammatory reaction may start, and thus favor infection. Probably phagocytes play an important part in all tubercular infections, carrying the non-motile bacilli into the tissues and setting them free to produce their specific lesions.

In the wall of the bronchus or alveolar passage so affected tubercles form which tend to spread in two directions, along the air passage, centrifugally, and into the lung tissue; the process becomes partly exudative as the alveoli about the bronchus become affected. Thus a series of little nodes, each with the lumen of bronchiole in the middle, is discovered on section, the centers caseous and a zone of pneumonia surrounding the whole. Of course the true form is rather that of a ball or spheroid, presenting zones only on section. This distinguishing

appearance of the lesion deserves the name of *disseminated tubercular broncho-pneumonia.*

In the miliary form of tuberculosis the new-formed tissue is for a time protected from the entrance of pyogenic germs. In the bronchogenic form it is the regular and inevitable sequel to have a secondary infection with pus organisms, and the foci of disease soon begin to break down and soften under suppuration. The large amount of sputa reinfects other portions of the lung and the clinical course of this "stage of softening"

FIG. 91.

TUBERCULOUS BRONCHO-PNEUMONIA IN THE UPPER PART OF THE LOWER LOBE. (*Ribbert.*)

The grouping of the lesions in relation to bronchi is clear.

is marked by a great increase in the gravity of the symptoms. Such a course may not be followed in favorable circumstances, for a common experience in post-mortem examinations is to find small areas where such a process has become latent, chiefly in the apex of one or both lungs, the tubercular focus surrounded by a thick capsule of new connective tissue. This is called "healed" tubercle and in many cases is practically so, but fresh infection from such a point is not uncommon. In other cases, where we may assume a single and limited infection, perhaps of attenuated bacilli, the course of the disease is

very slow, though many tubercles be present throughout the lungs. Of all parts of the lung the apex is most frequently the seat of tubercular processes, partly because the usual and slovenly method of breathing does not fill this portion of the organ with each inspiration, and partly because the bronchi come off at such angles that they are easily obstructed by secretion, and perhaps because the part is not so well supplied with blood as the rest of the lung.

Whatever the seat of the tubercular process, the regular development goes on slowly or quickly, with the softening and expectoration of the diseased tissue and the formation of cavities. The tubercle is non-vascular, owing to hyaline degeneration of the vessel walls of the part and the formation of thrombi, and hence degenerative changes are particularly liable to occur. Some of the cavities, however, are bronchiectatic, for the diseased bronchial wall yields to the air pressure and the traction of fibrous tissue in proportion as the respiratory efforts are increased. Across the larger cavities, which contain semifluid and purulent material unless communicating freely with a bronchus, strands of firm tissue run which represent fibrous bands of stroma and also vessels, converted into fibrous cords by organized thrombi. Because of the obliteration of the larger vessels, hemorrhage from the lungs is not common in the more chronic cases, occuring only when a vessel ulcerates before a thrombus has time to form and organize. The wall of the cavity is usually set with small tubercles and groups of them, and hanging from it are shreds of necrotic tissue. By destruction of intervening walls several cavities may unite to convert a whole lobe into communicating caverns, with strands and projections across them of fibrous nature. The fluid in such cavities may contain no bacilli, or none which may be stained; they require injection into a sensitive animal at times before they can be recovered. The size of the cavities and the number of them correspond fairly well with the clinical course of the disease, acute cases showing many small ones scattered

all through one or both lungs. Such a case often develops from an unresolved pneumonia, especially of the apex, which has become infected by many tubercle bacilli.

The converse of this is equally true, a lung which is already the seat of tubercle and cavity formation may secondarily become the seat of lobar pneumonia, which differs not at all from lobar pneumonia in non-tubercular lungs. Such a case should not be called tubercular pneumonia, but rather what it is, lobar pneumonia in a tuberculous lung. These cases are common in hospital patients in winter. It is not uncommon to have such a terminal pneumonia in portions of the lung which are still free, while the rest shows all varieties of tubercular infection, and, while commonly of the fibrinous form, it may be catarrhal.

The commonest complications of lung tuberculosis are those of general depression, anemia and emaciation, and secondary infections in various organs. The alimentary canal is in danger from sputa which are swallowed,[1] the larynx is affected in a similar way, the pleura shares in the tubercular process either acutely or chronically, the lymph nodes of the thorax seldom escape, and when a pulmonary vein is infected any organ of the body may receive and develop the bacilli thus entering the circulation. Intercurrent pneumonia and nephritis are common. Where the lung is infected secondarily to other organs the original seat of the process, as in the prostate gland, may remain quiescent, or the fatal termination of the case may be due to the primary rather than to the secondary disease, as in the intestinal forms.

*Syphilis.*—In the new-born with congenital syphilis the lungs may share in the condition with other parts, as the liver, spleen, pancreas, epiphyses, etc. In the adult the diagnosis is not always easy, for the case seldom comes to observation till it has existed for long periods.

[1] Eighty per cent. of adult cases have intestinal lesions; about thirty-eight per cent. of children.

Congenital syphilis of the lung occurs as localized gumma, in a diffuse form, and in combinations of these. The diffuse may affect an entire lobe or the major part of it, giving it increased firmness and volume and a pale color. The microscope demonstrates a thickening of the stroma of the organ, both in the interlobular and alveolar septa, from the invasion of round and spindle cells. The vessels show uniformly a thickening of their walls, especially of the intima and media, and consequent decrease or destruction of their lumina; this explains the general anemia which has suggested the name "white pneumonia" for the process. By pressure of the new-formed tissue the alveoli are crowded together and they may be filled with desquamated epithelia; the distribution of the lesion is often lobular and peribronchial. The tissue of the lung and of the other organs contains many deeply staining cells which are thought to be altered red cells. Circumscribed gummata do not differ materially from the preceding except in the spherical form of the focus and the greater tendency to caseous degeneration. Such gummata may be under the pleura or more centrally placed, most often in the lower lobes; in size they vary from one-half to several millimeters in diameter and, at first soft and white, tend to become firmer and more yellow with time; the center may be caseous or softer. A zone of inflammation may surround them.

In the adult the histological changes practically are the same. They show the same tendency to occupy the lower lobes and the right lung is more often the seat of the gumma than the left. The chief diagnostic points are that the gumma does not tend to liquefy under the attack of pyogenic organisms and that in it no tubercle bacilli can be found; while tubercular foci will, almost without exception, reward careful search with the presence of the bacillus, or it may be regained by inoculation of animals. Microscopically the gumma presents obliterating arteritis and phlebitis, and transitions from firm fibrous tissue to granulation tissue richly provided with round and spindle

cells. When such a gumma becomes secondarily infected with tubercle bacilli the diagnosis is especially difficult. Softening gummata may cause cavities to form, and after the fluid material has been expectorated the cavity may contract and be obliterated by fibrous tissue; this distorts the lung, causing the pleural surface to dimple and changing the normal lobed appearance. The disease may be complicated by any form of bronchitis, pneumonia or tuberculosis.

*Glanders.*—The bacillus mallei may enter the lungs by way of the bronchi or by the vessels after systemic infection through the skin (the usual way). In the first case the inspired bacilli form small nodules in a lobular distribution, of a gray or pale yellow hue, soft and purulent if recent, at times caseous when older, each surrounded by cellular infiltration and punctate hemorrhages. The embolic or metastatic forms resemble the miliary abscesses of pyemia, occur in the lower lobes chiefly and are often surrounded by hemorrhagic pneumonia. In either case the entire lung may be affected or only a small section of it.

*Actinomycosis.*—Primary actinomycosis is less common than secondary. It may follow aspiration of the organism by itself or foreign bodies (as grain) infected with it. As a secondary disease it is due to rupture of an actinomyces abscess in the upper air passages or about the mouth, or the infection passes over from adjacent structures (mediastinum). In the latter case there is usually a single cavity, or a group of them, at the site of infection, containing thick purulent semifluid substance which contains small yellow points of fungus. Or, in the other modes of infection the distribution is more general and lobular, each nodule of indurated tissue is surrounded by pneumonia, often hemorrhagic, and tends to soften in the center; fibrous hyperplasia about these may make the resemblance to tubercle very striking.

**Parasites.**—The lung may contain fission fungi of various kinds, as already mentioned; two forms of aspergillus (niger

and fumigatus) give rise to a rare pneumomycosis aspergillina or exist as harmless inmates of tubercular cavities; mucor mucedo has also been discovered, and various yeast forms in connection with carcinomata. Among the animal parasites cysticercus cellulosæ, strongylus and distoma hematobium occasionally occur; the latter causes a chronic hemoptysis in certain parts of the world (Japan, Korea, Egypt).

## The Pleura.

**Circulatory Disorders.**—Independent changes in the vascular supply of the pleura can hardly occur, except perhaps in the parietal layer; these may be temporary and reflex from the thorax, on the principle that the vessels which supply a serous membrane supply also the integument over it. Practical application of this is made in the use of blisters and poultices to the chest. The visceral layer shares in anemia and congestion of the lung, stasis may lead to punctiform hemorrhages and the same occur in certain violent deaths, as hanging and choking; also in fevers and constitutional disorders with hemolysis. The cavity of the pleura may contain blood from wounds of either layer, bursting of aneurysms and perforation of tubercular and other ulcerative processes; this is called *hemo-*, or *hematothorax*. The blood may be partially absorbed, partly coagulated and organized, or the bacteria mingled with it may set up various forms of inflammation.

*Hydrothorax* is the name given to the accumulation of serum in the cavity, not accompanied by inflammation. This often occurs as part of a general dropsical condition, and slight degrees are commonly associated with the end of nephritis and other chronic diseases. Acutely formed it may be due to sudden interference with either respiration or circulation, as in carbon monoxide poisoning. The two layers of the pleura are edematous, their lymph channels are dilated and the endothelial cells are swollen or desquamating; the lung may be compressed and

even atelectatic if the amount of fluid is large and has been long present. The serum is clear and light yellow, or it may be slightly turbid from admixture of cells, and fibrinous coagula are found in it; the amount varies from a few c. c. to a liter or more (12 l. in a case recently seen).

*Pneumothorax* occurs when air enters the pleural cavity after perforation of either wall of the serous membrane, by tubercular processes, gangrene and abscess in the lung, rupture of emphysematous alveoli, perforation of the lung by purulent pleuritis, perforation by gastric ulcer, penetrating wounds of the chest. The tear may be round and with thinned or thickened edges, or linear; clear or partly covered with fibrin; large enough to be found readily by gross inspection or requiring a strong hand lens. The lung, unless held by adhesions, may be collapsed. When the cavity is opened the air rushes out with a hiss anw forms bubbles if opened under water. The tension of the air pushes the other lung aside and the diaphragm downward, the intercostal spaces bulge and the entire half of the thorax is in expansion. When the condition persists, suppuration of the pleura, because of the bacteria present, converts the condition into *pyo-pneumothorax*.

**Inflammation.**—The pleura shares in the inflammations of the thoracic organs and walls, or is attacked in the course of general infections (acute articular rheumatism, typhoid), or becomes secondarily involved when the pericardium or the peritoneum is the seat of inflammation.

*Pleuritis* may be exudative, all proportions of serum, fibrin and pus occuring in the exudate. When fibrin predominates it is called *dry pleurisy* or *adhesive;* if the serum predominates it is called *pleurisy with effusion;* when the exudate is purulent it is named *empyema;* one and the same inflammation may pass through all these stages. Pleurisy begins with acute hyperemia, at times so marked as to cause petechial hemorrhages. The membrane soon loses its glistening appearance, becomes opaque and covered with a delicate film of fibrin, holding a few leu-

cocytes in its meshes. This fibrinous coat may practically cover the entire surface of the lung and dip in between its lobes, fastening them together, or it remains in scattered patches. When the serous exudate is scant adhesions form between the two layers of the pleura, especially in the dome of the cavity. The serum is clear or blood-tinged. In some cases it accumulates rapidly till the thoracic contents suffer from the pressure. In the exudate there are always both red and white cells from the blood, but from the first, or after a time, the purulent element may exceed the others and the disease becomes empyema.

Beside the cellular elements the exudate regularly contains urea, uric acid and cholesterin; in the diabetic, sugar also may be present. The exudate may remain for a long time in the cavity and at last be reabsorbed, or turn purulent. In the latter case the fibrinous layer on the pleura becomes infiltrated with pus cells and is called a *pyogenic membrane,* pus being continually added to the exudate from its internal surface. If the exudate is removed, by absorption or operation, the two layers of the pleura may become adherent over a greater or less extent, forming a dense white layer which at times obliterates the cavity; the vessels of the adhesions and false ligaments so formed are sometimes so numerous as to relieve circulatory disturbances in the lung.

*Empyema, pyothorax,* usually develops from the sero-fibrinous form of pleurisy, unless lighted up suddenly by entrance of pus into the cavity from abscess of the lung or thorax wall. The pus is yellow, grayish or green, acid in reaction, and later may be mixed with blood from thin-walled new vessels. It perforates and escapes through lung tissue and bronchi, into the abdomen, or externally. It may decompose either with or without communication with the air. Empyema accompanies carcinoma and gangrene of the lung, diabetes and pleural tuberculosis.

The results of pleurisy depend chiefly upon the amount and disposition of the exudate, also upon the variety. Dry pleurisy

may be healed with adhesions of slight extent or larger and firmer ones; these restrict the movement of the lungs and if firm may contract the chest and lower the shoulder of that side. The adherent pleura may become extremely thick and its contracting force is marked and continuous; calcified plates may form in it. Between the lobes adhesions may be of little moment, or the starting point of tubercular infection. When serum is poured out in quantity it may be absorbed and the process ends as above, or it may become purulent and remain dormant, or cause symptoms of general intoxication. If it escapes by the bronchi, or externally, only adhesions and distortions remain, or a fistulous tract discharges indefinitely. In less favorable cases pulmonary abscesses and gangrene occur and end fatally.

**Tumors.**—Fibroma and lipoma may develop on the parietal layer, and chrondroma and osteoma also; less often they occur in the visceral layer. Endothelioma may begin in the lymph channels and infiltrate a large section of the pleura, resembling in gross appearance the simple fibrous adhesions left by inflammation, or it occurs as small nodes and spheres scattered over a less thickened surface; the cavity may contain serum and fibrin. Metastases are found in the lymph nodes of the thorax, in the lung and liver. Secondary tumors are especially common with malignant disease of the mammary gland, passing to the pleura through the anterior chest wall or through the lymph vessels, or as a series of interrupted nodules not connected with the primary tumor.

**Infectious Granulomata.**—*Tuberculosis* of the pleura follows similar affections of the lung or at times is a primary infection; even in many of these seemingly primary cases careful examination of the apex of the lung or of the bronchial glands will disclose the focus from which the infection came. The form is usually fibrinous, the hyperemic pleura with tubercles scattered over it being covered with a layer of fibrin and pus cells in varying proportions; frequently there are small

hemorrhages here and there. At times an ordinary pleurisy runs its course and afterward tubercles, lying till then latent under the pleura, become active and set up a tubercular inflammation.

Syphilitic pleurisy occurs almost without exception as an unimportant part of a general disease; it may take origin from subpleural gumma of the lungs.

# CHAPTER XV.

## THE DUCTLESS GLANDS.

### The Thyroid Gland.

**Malformations.**—Entire absence of the gland has been noticed in some cases of cretinism. Variations in its size and the number and disposition of its lobes are common, accessory thyroids occur near by or remote from the main gland, as behind the pharynx and lying on the arch of the aorta.

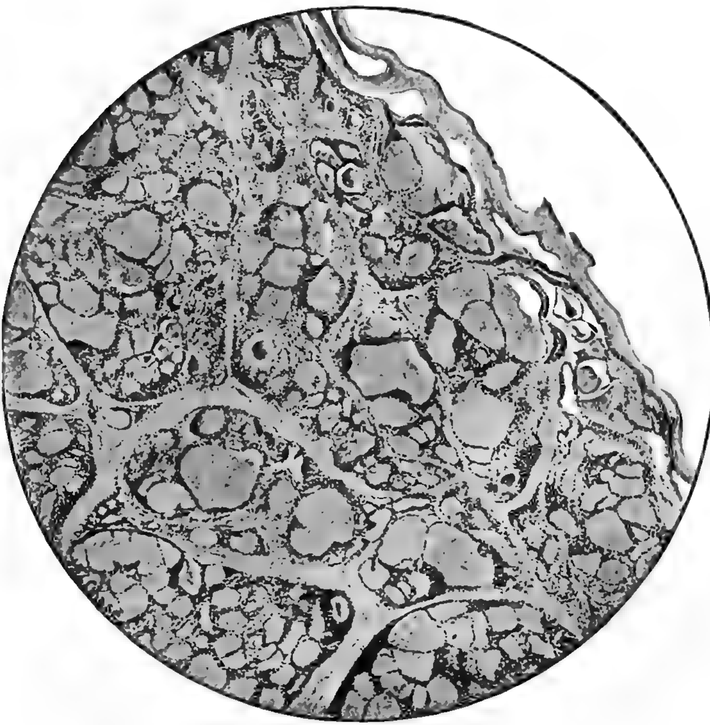
**Circulatory Disorders.**—*Active hyperemia* is favored by the free vascular supply and occurs especially in women, with swelling of the part; from repeated congestion the gland may enlarge (goitre), and this occurs alone or as a symptom in Graves' disease. *Passive congestion* may be the result of heart disease.

**Inflammation** is not common. It may follow any exciting cause of inflammatory reaction and either resolve, form indurations or suppurate; the latter in the form of miliary abscesses sometimes accompanies mycotic endocarditis. If the pus is confined by the gland capsule it may become thick and calcified; if it breaks through it follows the planes of cervical fascia into the mediastinum, or perforates the trachea, esophagus or integument. From the swelling and pressure it may interfere with respiration before this and cause death.

**Goitre.**—The thyroid is peculiarly liable to hyperplasia, the resulting tumor being known as *struma benigna* or *goitre.* This may be the result of repeated active hyperemia, or the connec-

tive tissue may proliferate, together with great increase in the colloid material always found in the gland lumina. It is difficult to separate simple hypertrophy of the thryoid from simple ade-

FIG. 92.



SIMPLE GOITRE. (*Stengel.*)
Dilated acini, containing colloid material, separated by bands of fibrous stroma.

noma and other enlargements of the organ. The name goitre is clinical rather than pathological and usually means simple hyperplasia. Struma benigna is divided into several secondary forms according to the gross appearance of the gland. It is

called *nodosa* when special areas appear hyperplastic, *diffusa* when the entire gland is enlarged, *adenomatosa* when the gland acini are numerous and larger than usual, *fibrosa* when there is evident excess of new fibrous stroma, and *cystica* when there are larger dilatations filled with colloid material. When colloid degeneration involves all the elements but the capsule a *colloid* variety is spoken of.

The results depend partly upon the size of the tumor but more upon the direction of its growth. Those which develop toward the integument reach a large size without giving any great annoyance; the same degree of growth toward the trachea compresses its lumen to a slit. When the thryoid passes in from the side between both esophagus and trachea it stops the passage of both food and air; if its main development is from the isthmus of the gland such compression effects appear early. Other structures which suffer from the pressure are the jugular vein, the carotid artery and the vagus nerve.

Except for the fact that goitre is endemic in certain countries and is believed to have something to do with the drinking water, its etiology is entirely unknown. Prolonged residence at high altitudes and constant intermarrying, are supposed to make goitre, dwarfing, and cretinism prevalent.

**Tumors.**—Apart from the forms of hypertrophy, fibroma and combinations of the same with sarcoma occur in the thyroid. Primary sarcoma is often of the round-celled variety, but may be spindle-celled; it is very malignant, invading adjacent tissues and forming rapid metastases. Carcinoma of the thyroid, *struma maligna*, is usually alveolar, starting in normal or hypertrophied gland tissue, rapidly invading the tissues of the neck and forming all into a single rather soft tumor. Degenerative changes are common in these cancers, fatty and colloid especially; less often the tumor becomes hard through the formation of fibrous tissue. Transitions from adenoma to carcinoma occur. Secondary tumors are uncommon.

Tubercles and syphilitic gummata have been found in the thyroid occasionally.

Simple degeneration, both colloid and calcareous, are at times described, and certain parasites have been found, as echinococcus and actinomyces.

The constitutional effects of thyroid disease are twofold, perhaps according to the absence or the excess of the gland's activity. In any case the relation of the gland to the nervous system is more evident than to the blood-making process, and it is permissible to think that it has a general control of important metabolic functions throughout the body. Thus when the thyroid is removed from young animals (rabbits) the bones cease to grow in length, and a similar observation has been made after operative removal in young children. Removal in the dog produces both nervous and nutritive disturbances, and in human myxedema the gland has been found markedly atrophied; it is known also, clinically, that artificial supply of thyroid gland lessens the symptoms of myxedema so long as it is kept up. On the contrary too much thyroid supplied will produce symptoms which strongly resemble exophthalmic goitre or Basedow's disease. In this there is evident hyperthyroidism, or overactivity of the gland, the rapid pulse, and bulging eyes and nervous symptoms being regarded as secondary to abnormal gland action; this disease has been considered as of strictly nervous origin, but the weight of evidence is against this view. In patients who have lost most or all of the thyroid a peculiar cachexia develops, called *cachexia strumipriva,* characterized by pallor of the surface, loss of hair, myxedema, weakness, and intellectual debility.

*Cretinism* is the name given to the condition of some children (especially in Switzerland) who suffer from thyroid disease (either atrophy or hypertrophy), imperfect growth and development, mental incapacity, swollen tongue and lips; the head is usually disproportionately large. The disease may be present at birth but more commonly it develops during the first year or

so, and more than one member of the family may be affected. Heredity is marked at times.

*Myxedema* is a condition of adult life, developing without apparent cause, with or without evident change in the thyroid, taking its name from the chief symptom, a swollen and firm state of the skin. All the layers seem to be infiltrated with some gelatinous substance; although the impression is that of edema it does not pit on pressure nor does it affect dependent portions especially. The swelling of the face and tongue, the change in the voice, the loss of mental power and the falling out of the hair, combine to alter the looks of a patient in comparatively a short time. The relation to the thyroid is evident from the effects of transplanting sheep's thyroid to the peritoneal cavity and administering the gland by the mouth. The hypotheses offered to explain the connection between thyroid and general disease vary between (1) a possible toxic influence from misdirected gland activity, (2) an excess of a normal product elaborated in the gland and delivered by the veins or lymphatics of the organ, which functionate as its ducts, and (3) a gastro-intestinal intoxication from impaired control over the metabolism of mucin. (See Pt. I., p. 57.)

## The Spleen.

**Malformations.**—Total absence of the spleen may occur in non-viable infants; the organ may be imperfectly divided by incisions along its sides; supernumerary spleens of small size are common.

**Displacements.**—Congenital or acquired conditions may be the cause of great displacement of the spleen. In complete situs inversus it may be found on the right side; hernia of the organ occurs through the anterior abdominal wall, or into the pleural cavity; increased volume of neighboring organs pushes it to one side or the other, fluid in the thorax and other causes of depressed diaphragm push the organ downward, food and

gas in the stomach push it up and back; its own weight may drag on its supporting ligaments so that it comes to lie in the pelvis on either side. A normal organ will not depart so far from its place, but after chronic congestion, as in malaria, some degree of dislocation is the rule. The vessels stretch and become dilated and tortuous, and if twisting occurs the organ may be atrophied or necrosed in its new location. It may also drag the fundus of the stomach out of place and produce compression of various parts of the intestinal canal.

**Circulatory Disorders.**—Anemia of the spleen is part of a general condition or follows great loss of blood. The organ is small and the capsule wrinkled, it is firm on section and no follicles may be visible, the stroma is somewhat prominent and the color is gray mixed with red. Recent embolism of certain vessels may produce a local anemia.

*Hyperemia* of the organ is physiological after the ingestion of food. Pathological hyperemia may occur in any acute disease of an infectious nature. The spleen is then swollen to several times its normal size, soft even to semifluid consistence, the stroma hidden in the swollen pulp, the capsule tense, even ruptured or breaking on gentle handling. Such increase in size and blood content is found in typhoid fever, anthrax infection, malaria, scarlet fever and diphtheria and some others of the acute fevers. Depending upon the length of time in which it is developed this swelling is wholly hyperemic and edematous or fibrosis coexists. The density of the organ corresponds, being firmer, often with marked thickening of the capsule, when slow fibrous changes have acted with hyperemia. The excess of blood may gradually subside and the lymphoid follicles increase in size and number, the color of the section is then gray or brown or red with lighter colored granules scattered through it and lines of increased stroma. Microscopically the spleen of infectious diseases presents many large and small mononuclear cells, polynuclear leucocytes mixed with these and countless red cells; late in the disease many of the cells are

swollen and cloudy. The hyperplastic organ shows many mitotic figures in the pulp and large mononuclear phagocytes with red cells englobed in them. The characteristic bacteria may often be recovered from the spleen, where they are in great part destroyed, either by phagocytic action or by antitoxic and antibacterial fluids. As a rule the swelling of the spleen gradually disappears after the disease has run its course, but it may not return to quite the normal size, the capsule may be permanently thickened and wrinkled, and the organ usually contains an excess of pigment.

*Passive hyperemia* and *stasis* often depend upon liver conditions which prevent the complete and rapid emptying of the splenic vein; to a slighter degree emphysema and valvular heart disease produce the same result. The condition is known as cyanotic induration. The corresponding changes in the organ are a dull blue color, increase in size and consistence, thickening of the stroma and vessel walls throughout, and, upon contraction of the fibrous tissue, distortion of the organ.

*Hemorrhage* may occur in the organ itself after injury or as red infarction; infectious disease with rapid increase in size of the spleen may be accompanied by small bleedings. Loss of blood from the organ follows traumatic rupture when much swollen, as seen in the large spleen of malaria, after comparatively gentle blows upon the tissues over it, or sudden extreme flexion of the trunk and compression of the spleen. A spontaneous rupture may occur with sudden hyperemia, especially when thickenings in the capsule prevent the expansion of the organ as in old people. The usual result is death after the effusion of large quantities of blood into the peritoneum.

*Infarcts* may be red or white, septic or not, and are very common in the spleen because the anastomosis between the ends of the splenic arterial branches are so few. The veins are large and anastomose freely, hence the red infarct is more common than the white. If infected, the wedge-shaped area, which always has its base under the capsule and its apex toward the

hilum, rapidly breaks down into an abscess, and this may rupture into the peritoneum and set up general or local inflammation. The size of the infarct varies with the vessel in which the embolus lodges; it may be relatively very large, and there may be more than one. Simple infarcts may be absorbed in part and encapsuled by fibrous tissue, leaving only a somewhat stellate scar to mark the site; when the red infarct heals the hemoglobin passes through various stages of decolorization and even in the scar leaves some trace of pigment.

FIG. 93.

TWO INFARCTS OF THE SPLEEN. (*Ribbert.*)
**Each surrounded by a line of hyperemia and bulging slightly above the surface.**

*Thrombosis* of the splenic vein may follow a similar process in the larger branches of the portal vein; it results in marked stasis in the organ. The splenic artery is often the seat of atheromatous changes and the nutrition of the part may suffer in consequence.

**Inflammation.**—*Splenitis* may be acute or chronic, localized or diffuse. The diffuse form is practically but a severe grade of the hyperemic swelling which occurs in infectious disease. The organ may reach five times its usual weight, it is soft, even semifluid, dark red on section at first and later of a paler color. Degenerative changes may go on in the pulp while fibrous hyperplasia proceeds in the stroma; the relative proportion of these determines the soft or denser consistence. Usually complete resolution is the termination of the process, but fibrosis, with permanent increase in size, or abscess formation and

rupture, may be the results. In the form of circumscribed abscesses an "idiopathic splenitis" may arise after pus organisms enter the blood current; the resistance of the organ may already have been reduced by general disease and its toxin (typhoid). Septic emboli also produce multiple small abscesses in the spleen, as in malignant endocarditis, pyemia and severe typhoid. In size these abscesses may be punctate or several centimeters in diameter.

*Chronic splenitis* is almost always diffuse, produced in the course of chronic venous congestion from cirrhosis of the liver or valvular cardiac disease; it may also follow the acute form after infectious disease, and of these malaria is most commonly observed. Early in malarial disease the spleen is soft, dark red and swollen; later it shows diffuse hyperplasia of the stroma, thickening of the capsule, and pigmentation of a deep brownish tinge; the microscopic appearances correspond. The final stage of such fibrosis is contraction, as elsewhere, and the spleen is then very firm, pigmented, capsule thickened in patches and much wrinkled, showing that it has been larger. On section the bands of fibrous tissue make a network through the organ, the veins are narrowed and the lymphoid elements markedly atrophied.

**Leukemic Hyperplasia.**—In the *splenic* form of *leukemia* the organ undergoes a marked hyperplasia, probably starting in the usual way as hyperemic swelling, and in time the volume of the spleen may be fifty or more times the normal, the weight as much as 8-10 kilos. The first stage of the leukemic spleen is fairly soft and on the cut surface there is a seeming division into regions corresponding to the end distribution of arterial branches, slightly bulging and marked off by lines of stroma. Microscopically the blood-vessels are dilated and red cells occur in the pulp. Malpighian bodies and fibrous elements are hyperplastic. In the second stage there is evidence of granular degeneration in the pulp, and pigment granules gather about the Malpighian corpuscles; here and there anemic necrosis follows

thrombus formation in the vessels. The gross appearance is a hardened organ with a much mottled surface, the capsule thickened irregularly, perhaps adherent to adjacent tissues, and the heavy organ is displaced, usually downward. See p. 372.

In *pseudo-leukemia, Hodgkin's disease,* the gross and microscopic findings in the spleen are almost identical with those of leukemia; from the organ alone it is hardly possible to make a diagnosis. Clinically there is more rapid hyperplasia of the lymph nodes and the blood examination is characteristic.

Operative removal of the spleen in dogs is followed by emotional disturbances, especially chronic anger. In the human subject splenectomy is remarkably well tolerated, perhaps because its blood-making function is performed by the marrow.

**Tumors.**—Primary neoplasms of the spleen are unçommon. Fibroma and angioma have been found. Among secondary tumors of malignant character sarcoma is least unusual, often melano-sarcoma; carcinoma may occur with general carcinomatosis and by extension from near-by tumors.

**Infectious Granulomata.**—*Tubercles* develop in the spleen as fine translucent points which resemble hypertrophied Malpighian bodies, but differ from them in their gray color, their abundance, firm attachment, and sharper definition from the pulp. In some cases there are large cheesy compound tubercles, as in chronic forms of the disease in children.

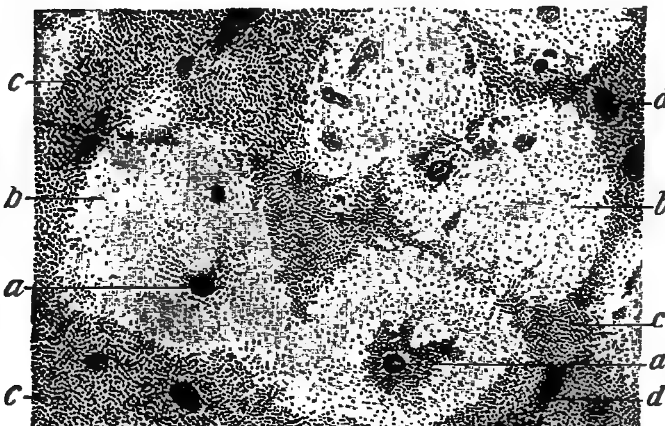
*Syphilis* produces increase in the size of the spleen, hardness of its tissue, and occasional gummata, miliary and numerous or single and larger.

**Degeneration.**—In the early years of senility the spleen begins to *atrophy* and this goes on more rapidly than in other parts of the body. The capsule becomes very thick, sometimes in patches, the lymphoid elements disappear, the fibrous are relatively more prominent and hence the organ is firm and small, its color brownish-red, and it is dry and pigmented.

*Amyloid* degeneration is often most marked in the spleen or even limited to this organ. If the Malpighian bodies are spe-

cially affected they stand out above the cut surface as grayish translucent granules, resembling boiled sago grains and hence the name "sago" spleen. If the whole organ is involved it reaches a large size, its edges are rounded, consistence firm; the cut surface is anemic, dry, both firm and friable, and in color a peculiar red like that of fresh ham. By the iodine test the lymphoid elements become more prominent or the whole cut

FIG. 94.




AMYLOID DEGENERATION OF THE SPLEEN. (*Ziegler.*)

*a*, transverse sections of the splenic arteries; *b*, amyloid areas; *c*, spleen pulp; *d*, trabeculæ.

surface takes on the reddish tinge. Microscopically the degeneration begins in the walls of the capillaries and small arteries, converting them into structureless amyloid tubes, and between the thickened lines of stroma lie clumps of amyloid matter; few cells remain.

*Pigmentation* occurs in anthracosis when the foreign dust passes the bronchial nodes, by ulceration into a vein for in-

stance; but the most common form is the deposit of malarial pigment, by which the organ may become dark brown to black on the cut surface. It results in part from destruction of red cells in the circulation and in part from their degeneration within the spleen.

*Calcification* occurs in the thickened capsule in old infarcts and in caseous foci.

Among parasites pentastomum denticulatum,[1] echinococcus and actinomyces are the commonest; all are rare.

## The Thymus Gland.

**Malformation.**—In some cases the gland is extremely small or even absent, the latter with marked defect of other parts; or it may be large enough to reach deep into the mediastinum over the pericardium, or its division into lobules may be especially clear. Normally it begins to atrophy by the second year by a process of replacement of fat tissue, though traces of the gland may persist till the twenty-fifth year.

*Hyperemia* may be found in the new-born and punctate hemorrhages when death has been due to asphyxia. *Inflammation* is very rare and is usually limited to a localized abscess; these may be multiple after infection of the umbilical stump. In the *status lymphaticus* the gland shares with other lymph structures in the hyperplasia (see p. 434).

**Tumors** are occasionally found and among the malignant are angio- and lymphosarcoma.

*Tubercles* may invade the gland in general infection and, as in cases of congenital *syphilis,* caseous foci may occur.

## The Lymph Nodes.

**Circulatory Disorders.**—Normally these structures appear pale in color though their supply of blood is fairly copious; with *anemia* they are clearly much softer than usual and on

[1] Larva of P. tenoidies.

section dry. When *hyperemic* they are swollen; the color is reddish and the section very moist; the hyperemia may be limited to the outer portion or the whole cut surface may bulge from increase in its contained fluids. Extravasated blood is common in the nodes of a part after injury of various kinds. *Pigmentation* of the nodes occurs locally after the extravasation of blood in the collection territory, after the introduction of foreign pigment as in tattooing, and in some diseases of the skin associated with anomalies of pigment formation, as in leucoderma syphilitica. Leucocytes are the chief carriers of the pigment but other cells with phagocytic powers assist. In the node the pigment granules lie in the lymphoid cells, in the stroma, or uniformly diffused. The result in marked degrees is impermeability for the lymph stream, so that it is directed to collateral channels and thus many nodes become tinged one after another, and also, if the foreign matter is irritating, the stroma of the nodes undergoes hyperplasia; if septic, ulceration follows.

**Inflammation.**—*Acute lymphadenitis* occurs most often from transport of microörganisms from peripheral traumatism, and the lesion is called primary when there is no inflammatory reaction at the seat of injury, mostly in superficial skin wounds, or secondary when it follows distal tissue inflammation. The first stage in the node is marked swelling and subjective tenderness, and as many of the prominent groups of nodes lie in the flexures of joints, large movements of the limb become painful. The swelling and hyperemia of the node give it a uniformly red and tumid look on section, and small points of hemorrhage may be found. Under the microscope all the spaces of the reticulum are stuffed with red cells and leucocytes, and while many of the latter are carried there from outside, others may be formed in situ, for mitotic figures are frequent in the round cells.

In favorable cases the evidences of inflammation disappear as quickly as they had developed; in others hyaline or fatty

degeneration occurs; when there are frequent accessions of irritating material the gland may become indurated from fibrous hyperplasia. The presence of pyogenic organisms determines suppuration and in the nodes an abscess forms, with suppuration in the perinodal tissues and perforation to the exterior. In the superficial nodes the pus does no further damage, the cavity granulates and heals, but in deep laid portions of the lymph system severe consequences may follow perforation into one of the great serous cavities, into the air passages or the circulation. Such a swollen lymph node is commonly known as a *bubo,* and while most frequent after distal lesions, as with chancre, erysipelas and skin wounds, buboes may occur with systemic infection as in bubonic plague. Scarlet fever and diphtheria with an added streptococcus infection are often accompanied by inflammation of cervical lymph ganglia, and anthrax may cause severe hemorrhagic inflammation, or even gangrene, in the nodes corresponding to the site of infection (See Lymphangitis, p. 364.)

The relation of many of the lymph ganglia to irritant and infectious substances may be regarded as a defense to the general system, for they filter out such sources of danger from the lymph stream and destroy them in situ, perhaps at the expense of suppuration.

*Chronic lymphadenitis* may follow frequent attacks of more acute type from recurring irritation and the nodes then are somewhat swollen, harder if the chief element is fibrous, softer if cellular increase coexists. Microscopically there are increase in the stroma with degeneration of the cells in the one case, and many round and epithelioid with some giant cells in the other.

**Tumors.** *Lymphoma, Lymphadenoma.*—While chronic hyperplasia follows chronic irritation, a more rapid increase in the elements and size of the lymph nodes, associated with similar changes in the spleen and variations in the composition of the blood, is observed in leukemia. The lymphatic form of that disease is characterized by great increase in the cells of the

lymph ganglia generally, with a less pronounced hyperplasia of their stroma and vessels. The gross appearance of the nodes will vary with the proportion of stroma and cells, but they are always larger than normal and at times the capsule is broken through and the neighboring tissues share in the hyperplasia. In the late stages of the disease not only all the lymph ganglia of the body are affected, but in places where normally there is no lymphoid tissue, as in the kidney and the liver, metastatic formations arise which suggest an analogy with malignant neoplasms. The usual place for the lesion to develop is in a group of the cervical nodes and from here it spreads to adjacent and then to distant groups.

When the blood fails to present the characteristic lesions of leukemia and only the lymph tumors develop, perhaps with splenic changes, it is known as *pseudo-leukemia* or *Hodgkin's disease*. The new tissue resembles sarcoma (round-celled) and develops in situations normally free from lymphoid structures; hence the name malignant lymphoma or lymphosarcoma of some observers (see p. 374).

The two forms noticed in leukemia are found here also, a soft tumor whose nature is chiefly cellular increase and degeneration, and a hard form with marked fibrous increase. In the former the ganglia appear swollen but distinct from one another, soft and even fluctuating, furnishing a milky juice on section, at times presenting small hemorrhages; in the other the nodes are not so large and much firmer, the cut surface is fibrous and of grayish or yellowish color. It is said that these pseudo-leukemic tumors differ from the leukemic in their larger size, in their tendency to involve adjacent structures, in the larger size of their cells with more frequent appearance of giant cells, and in the difficulty found in attempts to inject them by piercing the capsule with the injection needle. The degenerations which are common in the tumors depend upon compression of their vessels and are caseous or fatty most commonly.

*Myxoma* and *enchondroma* have been found in the lymph nodes but malignant tumors are more common. *Primary sarcoma* is sometimes seen, and differs from the "lymphosarcoma" mentioned above in its tendency to form metastases elsewhere than in lymph structures, while the other is confined to them at first. The sarcoma may be of any form but most often it is of the small round-celled variety; it usually starts in the fibrous structures of the ganglion, if fibro- or spindle-celled sarcoma. Melano- and angiosarcoma also occur, the former usually secondary. Of the secondary malignant tumors *carcinoma* is most frequent. Thus in carcinoma of the mammary gland the secondary manifestations in the ganglia of the axilla and the neck may appear very early, and reach a large size, even before the primary tumor reaches the skin and ulcerates. Examined early, the lymph nodes exhibit metastatic carcinoma cells among the normal elements of the part, though there is absolutely no gross evidence of participation; hence the importance of removing all adjacent lymph ganglia in operative procedures. In this case also the protective office of these nodes may be observed in the period of delay in metastasis in the early stages as neighboring groups become affected. (See Pt. I., p. 177.)

**Infectious Granulomata.** *Tuberculosis.*—In the local tuberculosis of the lymph nodes which is peculiarly marked in children before puberty, the infection most commonly occurs along the alimentary canal; perhaps from the use of infected milk, tubercular abscess in the udder of the cow being rather frequent and all the more dangerous because the animal's general condition does not suffer for a long time. Bacilli may pass into the milk even without disease of the udder.

The pathogenic action of bovine tubercle bacilli upon man has lately been denied. It must, however, be remembered that where it seems to appear, as a practical observation, the subject is usually an infant, whose lax tissues are less resistant than those of the adult. The infection, furthermore, is not simple,

Colon bacilli and others probably combine in the process, after the normal epithelial defence has been weakened by fermentation in the intestine.

The cervical nodes are often infected, in many cases through the tonsil, bacilli lodging in the crypts of this lymphoid tissue and being carried to cervical ganglia by phagocytes; the mesenteric nodes are infected in a similar manner and less frequently the bronchial. The node involved swells to a moderate degree, becomes hyperemic, paler after a time when hyperplasia follows, and then the central portions become caseous. As in the lung and other parts of the body, mixed infection by the pyogenic organisms frequently follows and the cheesy gland becomes an abscess, adhesions to adjacent tissues with perforation in the line of least resistance may follow. As in the neck, this is usually by external evacuation, and after a time the necrotic tissue is all extruded and stellate and irregular scars remain. If the pus is retained by a thick capsule it may dry and be infiltrated with lime salts. Secondary general infection is always possible from a lymph node where bacilli linger, especially when free entrance to the circulation is gained by adhesion with a vein and later perforation. Microscopically the lymph nodes present all stages of typical tubercular tissue and its degenerations, with bacilli in the giant cells or between the cells. After a time it is difficult to find bacilli in the ganglia, but they must be present, for injection of caseous or softened material from them into animals is usually successful.

*Syphilis.*—One of the first symptoms of constitutional infection is the indolent bubo. This may appear in either groin when the chancre is situated on the genitals, or in any corresponding node when extra-genital. The bubo is made up of nodes which are not very much swollen, but little painful or tender, and not given to suppuration; in these respects it differs from bubo following chancroid. In the secondary stage many or most of the superficial lymph ganglia are enlarged. After reaching a moderate development these nodal swellings remain un-

changed for long periods in the absence of antisyphilitic treatment. Microscopically they present thickening of the stroma and of the vessel walls, increase in the epithelioid cells of the sinus and the spindle cells of the stroma. In the tertiary stages gumma formation may occasionally occur in the lymph structures, but like all the severe forms of tertiary syphilis they are less and less frequent with the general tendency of the disease to run a milder course.

*Leprosy* causes fibrous hyperplasia, with fatty degeneration of the cellular elements, in the nodes corresponding to the skin lesion; later the internal nodes are also involved. *Glanders* produces swelling with small-celled infiltration.

**Degeneration.**—Simple atrophy is a constant accompaniment of senility, with cessation of the function. Fatty and amyloid degeneration occur at times, caseous changes with tuberculosis and syphilis, calcification as the final stage of these or after bone disease, as caries, with absorption.

**Status Lymphaticus.**—An unexplained relation exists between general lymphatic hyperplasia and certain sudden deaths, sometimes of adults but especially of children, and of great practical importance in connection with surgical anesthesia. Cases have been reported which had nothing to do with administration of an anesthetic, the child suddenly becoming cyanotic, with convulsions of the facial or trunk muscles, involuntary urination and defecation, and death in a few minutes. Perhaps the greater number, however, have occurred with the use of chloroform, often to but slight degrees of narcosis or sometimes afterward. On post-mortem examination the thymus is usually large, so that *thymic asthma* and *laryngospasm* were names formerly applied, but other lymphatic structures present similar gross appearances. The pharyngeal and faucial tonsils, the follicles at the base of the tongue, the lymphoid elements in spleen and intestine, and the systemic lymph nodes may all or most of them be enlarged. Associated aplasia of the aorta and entire arterial system, dilatation of the heart, and general deli-

cacy and imperfect development have been described. At times more than one member of a family has died in this condition, in anesthesia or apart from it. But little can be said of its causation or its significance. Altered products of the hyperplastic tissues have been assumed, which induce convulsion and syncope on slight stimulation. The tendency appears to be to outgrow it, but during the first years of life clinical experience has proved the wisdom of examining all accessible lymphoid tissues before administering chloroform, and withholding it in the presence of general hyperplasia.

Other lymphatic structures, as the tonsil and bone marrow, remain to be treated. The tonsil will be considered in connection with the alimentary canal. So far as the marrow requires special mention here, apart from diseases of bones, it is chiefly as alterations in the blood produce lesions in the marrow or the converse of this. Finely divided irritating and infectious material tends to collect in the marrow as in the spleen and lymph ganglia, and hence osteomyelitis is occasionally a complication of scarlet and typhoid fevers, variola and measles, malarial and pyemic infections. In pernicious anemia red marrow forms where usually only fatty marrow is found, perhaps in consequence of vicarious function when other blood-making organs are diseased. Normally red marrow occurs in the bones of the skull and the pelvis, the thorax and the proximal ends of the arm and thigh bones; in the latter situation fat takes the place of nearly all of this with the advance of age and in late years it becomes mucoid. When pathological influences reproduce the fetal red marrow it occurs centrifugally in the long bones, contrary to the physiological replacement of red by fatty marrow. In course of this change the fat cells disappear with the increase of lymphoid cells with large nuclei, red cells often nucleated, microcytes and poikilocytes, eosinophiles, myelocytes and giant cells which may contain red cells. The gross appearance of the marrow may be red and translucent (so-called "raspberry jelly") as in pernicious anemia, or

variously mottled from pink to gray, or yellow and puriform, or even greenish as in leukemia. Beside the cells mentioned the microscope discovers pigment and Charcot-Neumann crystals. At times the other lymph structures are relatively but little involved, or late in the disease, and hence a myelogenous leukemia is spoken of, in contrast to the lymphatic and the lienal or splenic (see pp. 372, 374).

## The Adrenal Body.

**Malformations** are not common; they include absence with marked general defect, fusion by a bridge of similar tissue, supplementary adrenals connected with the solar and renal plexuses, and dispersion of fragments in the liver, kidney and genital organs. From these hypernephroma may develop.

*Hemorrhage* in constitutional conditions may involve one or both organs and occurs at times in the new-born.

*Inflammation* is unusual; it may be purulent and either diffuse or localized.

*Tuberculous* disease is one of the commonest lesions of the part and is often the chief pathological find in Addison's disease; but it occurs also without any trace of pigmentation of the surface. The tubercles may be miliary or in caseous foci, cause increase in the size of the organ, rounding of its sharp margins, and usually are secondary.

*Syphilitic induration* may occur in a congenital form, and with gumma caseous degeneration may occur.

**Addison's disease, supra-renal melasma,** is a clinical complex of emaciation, anemia, muscular weakness and pigmentation of the skin and mucous membranes (mouth) of a peculiar metallic color, which has given the disease the name cutis aenea. The only pathological lesion in many cases is an adrenal lesion, which in some cases is absent, and, further, may occur independently of the other and general disease. Other pathological conditions which at times are associated

are sclerosis of the ganglia of the abdominal sympathetic, dilatation of its vessels and necrosis of the ganglion cells; in other cases pigmentation and fatty changes in these and other parts of the sympathetic. Experimental removal produces hemorrhage in the spinal cord and degeneration of nerves in animals; pigmentation seldom occurs and then is not surely the effect of the operation. The function of the gland appears to be the regulation of vaso-motor conditions rather than metabolic processes, and whether its lesions have a causal or necessary relation to pigmentation of the surface and cachexia is not wholly determined. (See Hypernephroma, p. 534.)

# CHAPTER XVI.

## THE DIGESTIVE SYSTEM — ALIMENTARY CANAL.

### The Mouth.

**Malformations.**—The commonest form of congenital imperfection in the development of parts about the mouth is fissure in the upper jaw, which may involve only the lip (hare-lip) or the bones, including the roof of the mouth; nasal, buccal and pharyngeal cavities then form one chamber. Such a fissure usually follows the suture between the premaxillary bone and superior maxilla; it may occur on both sides. The tongue may be too large or too small, or, as a great rarity, double; the lower jaw may be lacking, the lips may be fused or absent.

**Circulatory Disorders.**—*Anemia* of the lips and mucous membrane is a well-known symptom of general anemia. *Congestion* occurs in inflammation and early in certain infectious diseases, often with an eruption of the characteristic superficial lesion, even before it appears on the skin. *Passive congestion* is part of general cyanosis in lung and heart disease. *Bleeding* is common in purpura, scurvy and similar diseases.

**Inflammation.**— The developmental identity between the skin and the lining of the mouth is seen in the great similarity between inflammation in the one and the other; often the lesion passes from skin to mouth or *vice versa.* The process may be associated with free desquamation of the epithelium and sym-

pathetic excess of saliva; when the desquamation is severe shallow ulcers form. As in other superficial parts the inflammation may be simple and soon disappear, it may be more severe and accompanied with suppuration, or it may be chronic and result in fibrous hyperplasia and thickening of the part. A form of the latter is seen in ill-nourished children with nasal discharge, eczema of the upper lip and permanent increase in the thickness of the latter.

Acute inflammation of the entire mucous surface of the mouth is called *stomatitis* and may be of several kinds.

*Acute catarrhal stomatitis* occurs with irritation and injury from chemicals and hot fluids, with the eruption of the teeth and from excoriation by partly decayed teeth; in the latter form the trouble is more apt to be chronic, as is seen also in alcoholic dyspepsia. The desquamation may be slight or profuse: in later stages the epithelium proliferates without desquamating and forms areas of thick and white appearance, and at times the mucous glands enlarge and give a granular effect to the parts. The increased and altered saliva may deposit mineral salts on the teeth, and in the edges of ulcers, in severe attacks.

*Aphthous stomatitis, thrush,* is due to the growth of a fungus, oïdium albicans, through and between the superficial epithelia. The first stage is redness, then patches of white false membrane appear, attached firmly to the tissue beneath but later becoming loose. Beside the fungus and epithelial cells found in the membrane, many other forms of bacilli and cocci are present. From the anterior portion of the mouth cavity the fungus may spread to the pharynx and along the esophagus, invading parts covered with flat epithelium; less often where the cells are cylindrical. At times the parasite passes into the bronchi, and when there are superficial ulcerations on the skin these may also be invaded. The fungus may be cultivated on acid media and forms mycelial filaments when there is but little sugar present, with sugar the cells are chiefly round or oval and budding, like yeast (sac-

charomyces). It is improbable that the fungus can invade healthy epithelia; clinically it occurs only in the very debilitated, with neglected oral hygiene, and most commonly in young children. (See Pt. I., p. 211.)

*Vesicular* and *pustular inflammations* may occur in the mouth as on the skin, a good example of the latter being the pustules of variola and secondary syphilis, which at times occur in numbers on the soft palate and neighbornig parts.

*Scorbutus* affects the mouth as one of the characteristic points of attack. It may be the first part invaded, beginning with swelling and dusky hue about the teeth, bleeding on slight cause or spontaneously; the teeth become loose, the gums recede and ulcers appear on them; gangrene of soft parts, and entire loss of the teeth, with necrosis of the bones may result.

*Mercurial stomatitis* in persons with an idiosyncrasy may result from but trifling use of the drug; in others it comes on after long treatment with it. The teeth give pain when shut tight together, the saliva increases to many times the daily normal and has a foul odor, there is swelling in the cheeks and the gums, and here and along the tongue shallow ulcers form.

*Tubercular* invasion of the lips and tongue may occur as a primary lesion, as a papule with eroded surface and early formation of an ulcer with thickened edges. The color is at first yellowish, later the base of the ulcer is made of sluggish granulation tissue. The resemblance to epithelioma and softening gumma is so close that the tubercle bacilli should be found (most often in giant cells) before making a positive diagnosis.

*Syphilis* affects the mouth either as a primary lesion (chancre) on some part, as lip, tongue or tonsil; or as mucous patches and other secondary forms; or as gumma, most often in the corners of the mouth or on the palate. The gumma is apt to make severe ulcers as it softens and often perforates the velum or destroys the uvula.

*Actinomyces* is liable to invade parts about the mouth, but probably there must be some abrasion of the surface before it can cause important lesions; frequently through carious teeth the fungus reaches the alveolar border of the under jaw. Its course, wherever it settles, is either a rapid suppuration, which is not common, or a steady swelling and destruction of surrounding tissue with but little pus formation.

FIG. 95.

CASE OF NOMA. (*Stengel.*)

**Gangrene of the Cheek, Noma.**—Children debilitated from severe and chronic disease, in surroundings of dirt and imperfect supply of air and food, occasionally present a rapid form of buccal gangrene. It begins on the inside of either cheek as a

small blister with dark and foul contents. The skin reddens and then turns darker, vesicles form on the outside, the mucous membrane is bluish and livid, and the entire area becomes necrotic. The process invades the tissues in all directions, no line of demarcation forms, the cheek is perforated, and as far as the eyelid and the edge of the lower jaw all the tissue is dead; usually but one side is involved and the tongue is apt to escape. The usual result is death; in rare cases the edges of the part granulate and heal with a large scar. Although most common in female children under seven, noma has been observed at all ages and in either sex.

**Inflammation of the Tongue.** *Glossitis.*—Beside attacks of this disorder when other parts of the mouth are involved, it occurs by itself either as a superficial or a deep parenchymatous inflammation. The first may be the sign of widespread digestive disorders, associated with functional and organic disease of the liver or of any part of the intestinal canal, or it may follow local irritation as from tobacco, sharp edges of carious teeth, etc.

A chronic form of epithelial hyperplasia, often very circumscribed, is known as *psoriasis* of the tongue. The affected areas are thick and white, lie along the edges or on the upper surface of the tongue, may spread and join; sometimes the abnormal epithelium is cast off and a small ulcer is left. The disease is important clinically because of secondary development of epithelioma on the site of the ulcer.

Another form of superficial inflammation of the tongue is *melano-glossia* or black tongue, in which the filiform papillæ reach a remarkable size and give the upper surface a hairy appearance and a black color. The condition is explained as a hyperkeratosis with local increase of pigment, or as due to a fungus resembling oïdium albicans, which is almost always found mingled with the thickened epithelia and various bacterial forms.

Phlegmonous inflammation of the deeper tissues of the tongue differs from other suppurations but little and is due to similar causes; the end of the process may be a permanent increase in size. Tubercular and syphilitic ulceration may occur alone on the tongue or when other parts of the mouth are also involved.

**Tumors.**—Almost any of the benign tumors of the connective tissue group may occur in the mouth and seldom reach a large size; the mucous glands about the lips may hypertrophy and their lining cells undergo either hyaline or colloid changes; nevi and cavernous angioma are both observed, most often on the upper lip. Among the malignant tumors epithelioma of lip and tongue is most common. On the lip it usually comes on the under one and is laterally placed, affecting men almost exclusively. If superficial it ulcerates rapidly and soon invades the sublingual lymph nodes. On the tongue one or the other edge is marked by a grayish and dense area, slightly prominent, and soon afterward a rapidly spreading ulcer. While but one half of the tongue is usually affected the tumor spreads quickly to the gum, cheek or larynx, and because of lymphatic transportation its course is quick and return after operation frequent. Epulis is the name given to various tumors which start in the alveolar borders of the jaws; these may be benign fibromata, but most often are some form of sarcoma; giant cells are common in them. Osteosarcoma may spring from the outer aspect of the teeth and cause the lower jaw to develop to enormous size.

## The Teeth.

In number and size, variations of the teeth are common; supernumerary teeth and extra digits on hand or foot sometimes occur together in more than one of a family. When teeth of the first set remain too long the corresponding ones of the permanent series may be small or altogether absent. With congenital syphilis the incisors, especially the middle upper of the

second set, are excavated along the cutting edge in crescent form and the others may be peg-shaped or irregular, but this and the yellow hue of teeth have been found where syphilis could not be proved.

**Inflammation** may affect the periosteum of the tooth's insertion or gain entrance to the pulp cavity; in either case suppuration may occur, with death of the tooth. Chronic inflammation and caries of the teeth usually are due to destruction of the enamel by acid fermentation of particles of food left between the teeth; about sixteen kinds of bacteria living in the mouth may produce such fermentation. Through the destroyed enamel the tooth loses its mineral salts, bacteria invade the dentine tubules and the tooth becomes carious; this is the result of more than one kind of organism, a mixed infection, with cocci as the most numerous variety.

## Palate and Tonsil.

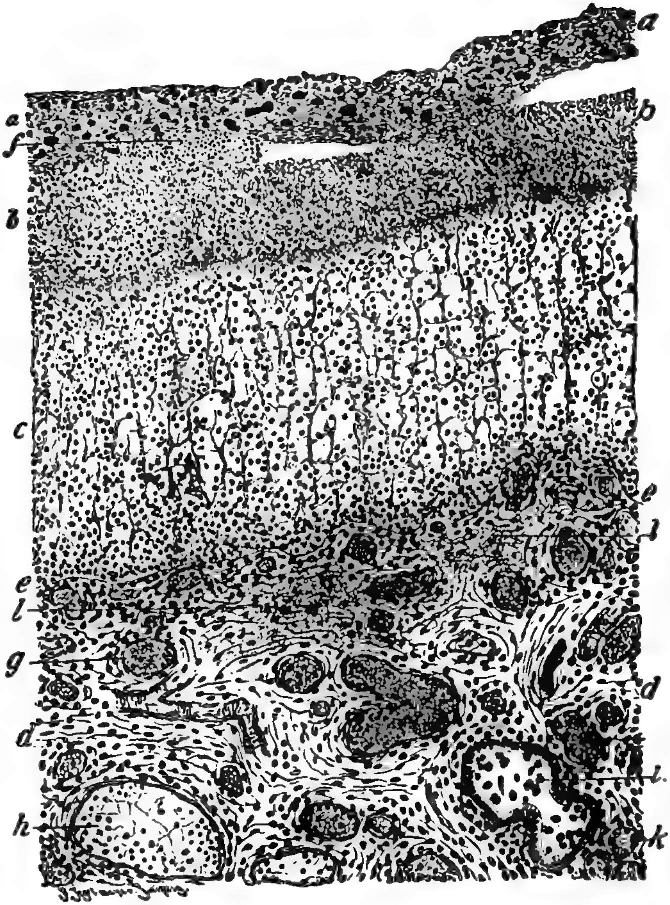
As in other situations, anemia and hyperemia follow such conditions in the body at large, acute congestion is seen in the first stage of inflammation, passive congestion with any condition of obstruction to the return circulation; in the latter case the veins of the part may be varicose. Hemorrhage may be caused by wounds, foreign bodies, and cachectic conditions; when the blood collects between the layers of the soft palate a large hematoma may form (staphylhematoma). Edema occurs with inflammation and ulceration and, because of the looseness of the tissue, may be very marked.

**Inflammation.**—The localization of the inflammation is diffuse, over the whole inner surface of the mouth and pharynx, or confined to the velum and uvula; it may be of any kind and is divided into symptomatic and idiopathic. The name given to these inflammations is *angina,* catarrhal, croupous, diphtheritic or phlegmonous according to its nature.

*Catarrhal angina* may be acute or chronic. In the former case it follows reflex or direct irritation and may be on the posterior surface of the velum and include the tonsil, or be variously circumscribed. The part is edematous and swollen, redder than normal, at times dotted over with swollen glands and these may be prominent from a drop of pus in each; such an appearance is common with the exanthemata. Vesicles may form, at times herpetic, and shallow ulcers from desquamation of edematous epithelia; when these latter cells are much swollen but remain attached they resemble the false membrane of diphtheria; under the microscope pus-cells are found inside the epithelia. In a chronic form such a simple angina may follow frequent attacks of the acute and a granular and varicose appearance is then characteristic.

*Diphtheritic Angina.*—Microscopically the croupous inflammations of the various mucous membranes are more superficial than diphtheritic, the pseudo-membrane, made up of desquamated epithelia, pus-cells and fibrin, lying upon the membrane; while in the diphtheritic inflammation the layers under the false membrane are necrotic, infiltrated with fibrin, and the resulting ulcer much deeper. Such inflammations in the palate occur after various injuries, chemical and other, and in the course of several acute diseases, scarlet fever, measles, variola and others. In all of these the exudative inflammatory products are mingled with pus and necrotic cells from the mucous surface. The characteristic lesion of diphtheria as a specific disease is a false membrane made up of two elements: fibrinous exudation, the fibrin lying between the dying or dead cells of the part, and coagulation necrosis even into the depth of the mucous membrane, with well-marked emigration of white cells and to a less extent of red. Such a false membrane is most often observed on the tonsils and the pillars of the fauces, but it may invade the nasal cavity (through the pharynx), the larynx and bronchi, and even the esophagus and stomach. At first its color is white or gray, at times with a yellow tinge, but if red

FIG. 96.

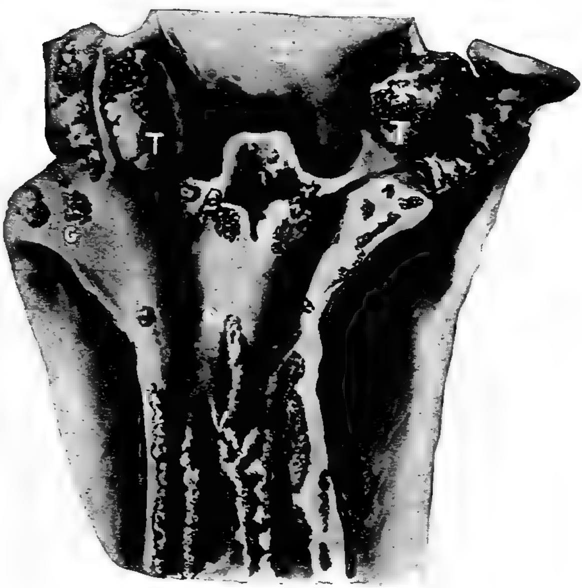



DIPHTHERITIC INFLAMMATION OF THE UVULA. (*Ziegler.*)

*a, b, c,* Three layers of fibrin, the upper containing groups of cocci, the others holding leucocytes in their meshes; *d,* connective tissue infiltrated with cells; *e,* boundary zone of submucous tissue, infiltrated with round cells; *f,* red cells in groups; *g,* dilated blood-vessels; *h,* dilated lymphatic, holding serum, fibrin and pus-cells; *k,* transverse section of a gland tubule; *l,* fibrin in the connective tissue.

cells are present in numbers it may be dark; later it turns yellow or grayish-green. It may be expelled in bits by efforts of coughing and renewed many times in the course of the disease, and there may be little foramina in it corresponding to gland openings, or projections which fitted into the lacunæ of the tonsil.

Fig. 97.




False Membrane in a Case of Scarlatina and Diphtheria. (*Ribbert*). The exudate is most copious over the right tonsil. Z, tongue; T, tonsil; G, pharyngeal wall; O, esophagus.

The amount and distribution of the membrane gives a suggestion of the gravity of the disease. In severe cases it forms rapidly and spreads into the pharynx and nose or downward. It is very often the fact in these severe cases that there is a mixed infection especially with streptococci, and hemorrhage

and gangrene are most frequent when this is marked. On the edge of the affected spot the epithelia may persist although covered by the growing membrane, but directly under it they are lost, for the fibrin lies between them in the place of the cement substance and thus their attachment is soon loosened. Whether the coagulation of the fibrin here precedes or follows the necrosis has been disputed, but the probability is that necrosis follows coagulation. The attachment of the pseudomembrane is closer over flat epithelia than over cylindrical but in either case is apt to be cast off in fairly large pieces, and the tissue under it ulcerates and heals with but little scar formation. The local swelling may be so great as to cause a stenosis.

When the lungs are also involved it is usually a lobular pneumonia, with a descending croupous bronchitis or without participation of the bronchi. The lymph nodes of the region about the angle of the jaw are usually swollen in proportion to the severity of the attack. Ascending infection may pass through the Eustachian tube and set up otitis media.

Perhaps as important as the local infection there is constitutional disturbance of all gradations; limited to a slight febrile reaction, or with symptoms of profound septicemia. The postmortem examination in severe cases reveals marked hyperemia of the kidney, interstitial edema and bleeding about the glomeruli, and cloudy degeneration of the epithelia. Similar degeneration of the heart muscle occurs and may be the immediate cause of death, after the disease has apparently run its course. In the spleen hyperemia with swollen lymphoid elements may occur. Paralysis of the velum is common after diphtheria but the paralysis may affect distant muscles also, as those of the eyes, larynx and diaphragm. The lesion in the muscles is usually an inflammatory small-celled infiltration between the fibers, with granular degeneration of the muscle cells; fatty changes follow rapidly. In the spinal cord hemorrhages and degeneration of the ganglion cells correspond and in some very severe cases there are multiple punctate hemorrhages in the mem-

branes of the brain and in the cortex, as also in liver, kidney and alimentary mucous membrane.

The exciting cause of diphtheria is the bacillus diphtheriæ of Löffler, which is constant in the false membranes of palate, nose, pharynx and bronchi, and may be recovered from affected tissues even before the pseudo-membrane is well formed. Similarly it may linger for weeks in the apparently cured, or occur in healthy members of a family when attending a case. It is probable that the bacillus does not attack a healthy mucous surface, and its most damaging results are effected by association with streptococci. The bacillus is about 3--4 $\mu$ long and slightly thicker than a tubercle bacillus; the end may be apparently swollen and more deeply stained than the middle part, slight bending and variations in length are common. They stain readily with methylene-blue. At first the specimen obtained by swabbing the throat with sterile absorbent cotton may be practically pure culture; later the streptococci may outnumber the bacilli. While often confined to the mucous surfaces the bacilli may be recovered from the lymph ganglia of the part, the lung, kidney, heart, blood, spleen and brain. Probably the general symptoms are due not so much to transported bacilli as to toxin absorbed from the primary affection, for filtered broth cultures reproduce them when injected into susceptible animals (dove, goat, guinea-pig).

When an animal has been dosed with increasing strengths of filtered culture, or with bacilli which at first are reduced in virulence, its serum becomes antitoxic, and when injected into a susceptible animal protects it against infection. More important for therapy, it is found that injection of such serum has a curative influence when the disease is beginning, most marked when given very early after infection. (Pt. I., p. 238.)

*Phlegmonous Angina.*—The severity of the inflammation is marked by the great hyperemia and edema of the tissues, and the infiltration by pus-cells. The tonsils may so increase in size as to block the entrance of the pharynx, and become so

painful that the jaws are held rigidly shut. Spread of the inflammation may cause fatal edema of the glottis. Various bacteria may produce such conditions, among them streptococcus and staphylococcus, pneumococcus, bac. mallei, and anthrax. Abscesses may form and discharge outwardly or into larynx or esophagus, and the affected parts may become gangrenous. Septicemia is to be expected and may be the cause of death.

*Tonsillitis.*—In any of the forms of inflammation about the palate the tonsils may be implicated and bear a large share of the damage, but frequently they are the only site of the lesion and several forms of *tonsillitis* are therefore described, which differ pathologically but little from those already mentioned. *Catarrhal, lacunar* or *follicular,* and *phlegmonous* tonsillitis are the usual forms.

Follicular inflammation may invade but a few of the crypts and remain at a low development for long periods, and as the bacterial elements present may be virulent, this bears a clinically important relation to diphtheria and tuberculosis. When the bottom of the crypt is weakened and perforated by the inflammatory process the severer forms of phlegmonous tonsillitis occur, one or both of these organs will be involved, considerable constitutional disturbance is usual, abscesses may form and break in varying directions and are most dangerous when involving the vessels of the neck or opening into the larynx.

A *chronic productive form* of tonsilitis results in great increase in the size of the part, and as the condition is often found in children, it is of great importance for their nutrition, for they are deprived of their normal supply of oxygen at every intake through the narrowed air passages, particularly so because they are apt to form the habit of mouth breathing, and their digestion suffers also. In these cases there may be simple lymphoid hyperplasia, as also in the vault of the pharynx, differing from the fibrosis which follows repeated acute tonsillitis.

*Tuberculosis* may affect the tonsil primarily and become generalized from here by way of the lymph channels to the lungs. *Syphilis* is found as primary lesion, secondary syphilide and gumma. *Lupus* occasionally is transmitted from the outer surface. *Glanders* nodules and leprosy tubercles are also found in palate and tonsil.

**Tumors.**—Lymphatic hyperplasia is common in the tonsil, either as primary or secondary lymphoma. Chronic inflammation of the mucous membrane sometimes results in polypoid formations. Papilloma, myoma and fibroma are sometimes found, and, among the malignant tumors, sarcoma and extensions of epithelioma.

## Pharynx and Esophagus.

**Malformations** are not common, and perhaps fistulæ from imperfect closure of a branchial cleft are the only ones of practical interest; it may be the second, third or fourth cleft, and the outer opening varies correspondingly. The fistula is complete between pharynx and external world or either end is closed, and such diverticula from the pharynx may be large and cystic. *Disorders in blood supply* follow those of neighboring parts and do not require special mention.

*Inflammation* follows injuries and extension from other parts and may be of any variety. Perhaps most common is the *chronic pharyngitis* of smokers and those who use the voice much, the mucous membrane being dry and granular, secretion scanty and viscid, vessels often varicose. Of the deeper inflammations *retropharyngeal abscess* is important, from caries of the cervical vertebræ most commonly, due to infection with tubercle bacilli. The end of the process varies with the acute or chronic nature of the abscess formation. The more rapidly formed are apt to bulge forward into the pharynx and rupture, while the slowly formed tend to follow fascial planes along the neck and perforate into the esophagus or bronchi or posterior mediastinum.

**Inflammation** of the esophagus follows swallowing of foreign bodies, hot fluids, acids and alkalies, and consists in some cases of hyperemia and desquamation, increased secretion being not demonstrable. In *chronic forms,* as in alcoholic patients, the mucous membrane is apt to be swollen and pigmented, of a brownish or grayish color, with small ulcers here and there; hypertrophy of the muscular layer, especially about the lower end, is often marked. *Suppurative inflammation* may come from the tearing and pressure of large foreign bodies or the ingestion of chemicals, as in attempted suicide, and the process may spread downward, dissecting between the coats of the tube.

As in the pharynx, *diphtheritic processes* occasionally spread from similar lesions in the mouth and nose. *Variola* produces its characteristic pustules and *thrush* spreads from the mouth.

**Changes in the lumen** of the esophagus are of great importance clinically, from interference with the function of the part. There may be uniform dilatation when the cardiac orifice is stenosed, increased in many cases by diaphragmatic action about the passage of the tube through it, the section just above becoming first involved; the muscular layers usually show well-developed hypertrophy in this condition. *Sacculated diverticula* are more important. If they result from pressure upon the wall from within they are called *pulsion diverticula;* if from adhesions and consequent pulling from without they are known as *traction diverticula.* The first is more common in the upper part of the tube, after loss of power in the muscular coat and hernial protrusion of the mucous. In form they resemble an oriole's nest, their lower portion being dilated and holding decomposed food, etc., communicating above by a narrow opening with the esophagus; the pressure of the dilated part may completely close the tube itself. The usual seat is the posterior wall at the pharyngeal junction, owing to the thinness of the muscularis mucosæ in this region and the horizontal arrangement of the fibers.

*Traction diverticula* are commonest about the bifurcation of the trachea, from adhesions of inflamed bronchial lymph nodes and consequent contractions of the new-formed tissue. The shape of the dilatation is conical, the apex lateral from the esophagus, and by hard particles of food or ulceration in the apex perforation may occur and a cavity form in the tissue, containing decomposed food and pus; this may break into adjacent air passages and cause gangrene of the lung, or into vessels with fatal hemorrhage.

*Perforation* and *rupture* of the esophagus may follow internal ulceration, and a peculiar form of this is found over the cricoid cartilage in states of extreme depression, or from external pressure by aneurysms and abscesses. Rupture has been described as the result of traumatism, or spontaneous. Regurgitation of gastric contents may partially digest the lower end of the tube and lead to perforation; since this may occur post mortem, care is needed in its interpretation.

*Tubercular, syphilitic* and *typhoid* ulcers have been described in the esophagus, but are unusual; their healing may lead to local stenosis.

**Tumors** of several kinds are observed here, but the most important is carcinoma, which especially affects men of alcoholic habits. The new growth is found in the lower or middle third, most often at their junction near the left bronchus. The tumor is usually disposed about the whole inner side as a ring and may not attain a great perpendicular extent. First the mucous coat is destroyed and appears elevated in papillary projections, with stenosis of the lumen; then the process involves the outer layers of the part and adjacent tissues, partly directly and partly through the lymph nodes. To this are added dilatation about the stricture, collection of food, ulceration and at times perforation. Metastasis is common in pleura, lung, and liver.

## Stomach.

**Malformations.**—The organ may be absent in non-viable infants, or as small as the duodenum, or contracted about the middle and hour-glass in form, or atresic at the pylorus. Various hernias may contain part of the stomach or all of it.

**Circulatory Disorders.**—The vessels of the stomach lie between the various coats of the organ, the arteries pierce the muscular layer at an acute angle, the veins are thin-walled and have no perivascular connective tissue, anastomoses are free and the total supply of blood is large to correspond with sudden functional demands; hence certain forms of variation in the blood contents of the organ are easily produced. *Anemia* with atrophy of the mucous surface occurs in long-standing anemic conditions and old age. *Hyperemia* is active and general (functional) during digestion, acute and distributed irregularly as the result of irritation; especially marked on the summits of the rugæ in the pyloric region. *Passive hyperemia* occurs with liver and heart disease and submucous punctate bleeding is then not uncommon. Similar small *hemorrhages* occur in many cadavers as the result of vomiting and other convulsive movements during the last minutes of life. If such a point of hemorrhage is examined by a side light a marked loss of substance in the epithelia over it may be made out. Central nervous lesions sometimes cause such small hemorrhages in the glandular layer, and also certain cachexiæ, as hemophilia and scurvy. *Massive bleeding* from the mucous membrane of the stomach occurs with ulceration, especially the round or perforating ulcer (*ulcus rotundum*) and gastric carcinoma. Rupture of passively congested veins is observed in cirrhosis of the liver. *Melena neonatorum* follows imperfect respiration and consequent backing up of the blood through the right side of the heart, vena cava and portal territory.

**Inflammation.**—*Acute gastritis* occurs from irritation of various kinds and is commonly located in the pyloric end. If

the irritant is a poison it may float over the food in the fundus and attack the pyloric region and duodenum without leaving any marked trace about the cardiac end, but taken on an empty stomach it may produce its effects in the fundus also. The mucous membrane is red and swollen, its secretion is increased and small bleedings under and in it are common. Convulsive contraction of the muscle layers may produce hour-glass forms. *Chronic inflammation* also is most evident in the pyloric end and here the mucous membrane may be prominently marked off into little polygonal areas, giving the surface a mammillated appearance; the mucous surface is often covered by a layer of thick mucus more or less firmly adherent. As a result of chronic inflammatory hyperplasia the mucous glands may atrophy, and the mucous layer be increased in thickness and pigmented. If the hyperplasia is localized one or several polypoid growths may reach a large size. All combinations of glandular, fibrous and polypoid hypertrophy occur, but in some cases the glands are chiefly atrophied and the new growth is fibrous, a condition known as *interstitial gastritis.* Such atrophic gastritis regularly occurs with cancer and ulcer of the organ, in a broadening zone about the main lesions. When the fibrous tissue reaches the state of contraction the mucous membrane may no longer be movable upon its supporting tissue and the lumen of the stomach is lessened, at the pylorus actually stenosed.

A *phlegmonous form* of *gastritis* occasionally results from injuries, chemical corrosion and progress of ulceration in the mucosa; then the submucous tissue and the intermuscular connective tissue are very edematous and later infiltrated with pus cells. When this proceeds to abscess formation and involves the major part of the organ the mucous layer seems to float on a purulent collection under it, or here and there it is necrotic and undermined and the lesion is more restricted. Malignant endocarditis and pyemia cause multiple *embolic ulcers* in the stomach walls, anthrax produces regional necroses with hem-

orrhage, and occasionally small-pox pustules are found. In rare cases diphtheritic inflammation has occurred with the same lesion higher up or in the course of severe infectious disease, as puerperal fever and variola.

**Round Ulcer of the Stomach.**—This is sometimes called *perforating ulcer* and sometimes *peptic ulcer* of the stomach. It differs from ulceration of other mucous surfaces and many explanations have been offered to account for its formation. One idea is that thrombosis occurs in a vessel and as a consequence a small area of mucous membrane undergoes necrosis, this necrosed portion is no longer able to resist the action of the gastric juice and is digested off, leaving an oblique, cone-shaped loss of substance, most marked in the mucous layer and gradually decreasing to the serosa. At the same time, if there were necrosis of the mucous surface and the dead tissue were being digested, the process would undoubtedly lead to formation of a thrombus in the vein below. Embolism and spastic contraction have been supposed to occur in the arteries, but as to the former the stomach arteries are not end arteries but anastomose freely, and such ulcers of the stomach do not occur specially often in embolic diseases, as endocarditis. Small hemorrhages in the mucous membrane from violent emesis may also cause the local death of the cells which permits the gastric juice to digest them, and possibly very hot drink may sometimes act in a similar way. The outline of the ulcer is usually round or pulled into an oval by the muscles, and when it perforates the serous coat the foramen looks cleanly punched out; the floor of it otherwise is pale and smooth, as are the edges also, but both may be swollen and firm. Such ulcers are usually small and single and situated on the posterior wall near the lesser curvature, about mid-way between cardiac and pyloric ends, but they may occur in any part and may be multiple and large. At times the ulceration opens a vessel of some size in its floor and fatal hemorrhage occurs. If the process heals, the scar may contract and distort the size and shape of the organ; ste-

nosis is most probable when this occurs at the pylorus. At times the serous coat is protected by adhesion to neighboring parts and then perforation occurs into the substance of adjacent organs or into hollow cavities, as the pleura, the transverse colon, or the peritoneal cavity, which latter may be fatal at once or after peritonitis. Gastric ulcer affects women more than men (about 75 per cent.) and before middle life. Cancer of the stomach sometimes develops from it.

**Degeneration.**—*Atrophy* results from chronic inflammation, affecting the glands principally, or occurs in pernicious anemia and old age. *Fatty degeneration* of the epithelial cells is one result of phosphorus-poisoning and is seen in some infectious diseases. *Amyloid* changes affect the stomach both in its mucous and its muscular layers, beginning, as so commonly, in the walls of the smaller arteries. *Pigment* is deposited in the mucous surface after hemorrhages and in the course of chronic malaria, and little areas of *calcareous* infiltration are sometimes seen with bone diseases.

*Gastromalacia* is always a post-mortem change, though in the older writings it is supposed to occur during life when the digestive power of the gastric juice is specially high and vasomotor action disturbs the blood supply. The softening of the digestive wall corresponds to the position of the body and is marked if the stomach is full of food and in warm weather: the appearance of the part varies, with the amount of blood in the stomach wall, from a pale gelatinous to a dark brown, the former especially in children and the latter in adults. The veins may appear as a dark network, most prominent in the fundus, and post-mortem imbibition of altered hemoglobin along them makes the lines broader. There is often perforation and the wall of the foramen shows not the slightest trace of inflammatory reaction.

**Infectious Granulomata.**—*Tuberculosis* of the mucous surface of the stomach is almost unknown, though fatty and other degenerations of its glands with tubercular disease elsewhere is

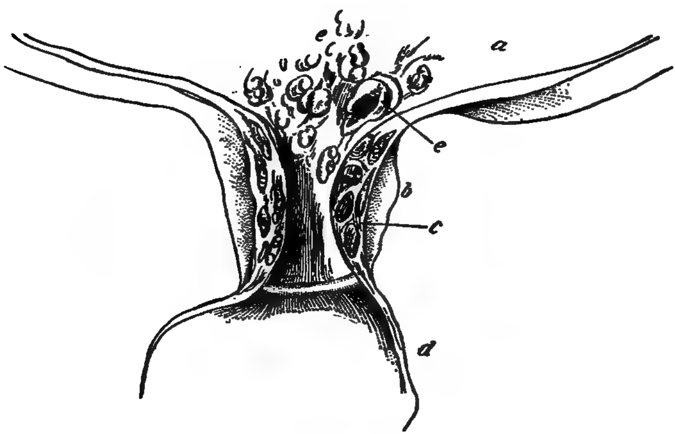
quite common; from the peritoneal surface it may, in rare cases, be affected. *Syphilis* occurs in a congenital form, at times associated with bleeding from the mucosa; gumma of the liver may produce stasis in the stomach veins or the latter may show gummatous infiltration. Occasionally in syphilitics a fibrous hyperplasia occurs all through the coats of the organ, and, by resulting contractions, the shape of it is much distorted. Rare cases of *actinomycosis* and *glanders* of the stomach have been reported.

**Tumors.**—None of the benign tumors are of much importance in the stomach, though fibroma and myoma may at times occur; sarcoma is a most unusual find; when present it may be either spindle-celled or fibro-sarcoma. Polypoid tumors of the mucous surface occasionally follow chronic inflammation and the larger ones are at times cystic. *Adenoma* occurs as a pedicled tumor, or diffusely spread through the wall; its mucous surface is apt to ulcerate. If typical adenoma, it is made up of glandular acini, with the membrana propria well preserved and usually but one layer of glandular epithelium covering it. Transitional forms to carcinoma are apt to be found with adenoma, and then with the still typical glands are mingled others which show one or more layers of cylindrical epithelium on their walls, but the lumen is filled with atypical epithelia. Such a tumor forms metastases, sometimes rapidly, in the lymph nodes about the smaller curvature or the omentum or in more distant organs; it is usually called *adenoma destruens* or adeno-carcinoma, and very often undergoes colloid degeneration. (Pt. I., p. 173.)

*Primary carcinoma* of the gastric mucosa is commoner in men than in women, on the anterior rather than the posterior wall, and after middle life. In all these points it differs from gastric ulcer, though it may take its origin from a healed ulcer (3 per cent. of all cases.). It appears in several forms and in the gross is either annular, often surrounding the pylorus; or parietal and localized, when a region of the wall is very thick

and presents an ulcer with raised firm edges; or it may be diffuse and involve half or the greater part of the organ. It is either medullary, alveolar, colloid, or scirrhous, the first of these growing very rapidly and with much ulceration, the latter more scar-like and slower in development. The ulcer is produced by necrosis of the epithelia as the result of locally altered nutrition, and while its thickened wall rapidly spreads in every direction

FIG. 98.




SCIRRHOUS CANCER AT THE PYLORUS. (After *Orth.*)

**Thickening of the walls and stenosis, dilatation of the stomach, ulceration of the neoplasm. *a*, the dilated stomach; *b*, the thickened pylorus; *c*, its wall cut through; *d*, the duodenum; *e*, nodules of neoplasm.**

its inner aspect continually breaks down; thus a large part of the mucous surface of the organ may be destroyed, large vessels opened and fatal hemorrhage produced. Less extensive ulceration may occur with the scirrhous form, and as the outline of this is usually round and its edges firm it may be easily mistaken for an ulcus rotundum; which fact together with the rather frequent development or carcinoma from a previous ulcer, makes

the gross diagnosis a matter of difficulty in some cases. In the diffuse form, usually scirrhous but sometimes colloid, the whole stomach wall is thick, its rugæ are permanently infiltrated and stretched flat, its surface is consequently smooth, pale and cicatricial. Microscopically much of the muscle coat is replaced by fibrous tissue, and here and there are small alveoli containing what is left of the atrophic epithelia.

Almost all varieties of cancer begin in the crypts of the mucosa, but they soon attack the submucosa and spread in all directions under the apparently unchanged mucous layer. Soon the muscular layer is passed and the serosa involved, with nodular and projecting masses of neoplasm. From here the whole peritoneum may become invaded, as is common in colloid cancer. Other forms of the neoplasm tend to perforate adjacent viscera, the pancreas, liver and colon especially. The adhesions between the stomach and surrounding parts may prevent escape of stomach contents, or perforation may make fistulous tracts communicating with the pleura or the transverse colon, the esophagus when the tumor is higher up or the duodenum when at the pyloric end. The lymph nodes about the site of the lesion are early involved, but others at a distance, as in the supra-clavicular region, may also enlarge. A third manner of spreading is found in the veins. These may be opened on the surface of the ulcer and carcinomatous thrombi form in them; bits from these are carried to the liver capillaries and wherever they lodge a secondary tumor starts which reproduces the original gastric tumor. Such metastases may be so rapid and reach so large a size that they entirely mask the still circumscribed gastric tumor.

**Gastric Dilatation.**—While stenosis of the pylorus may result in gastrectasia, it sometimes occurs while the pyloric ring is well preserved. When the muscular elements in the pyloric wall are hypertrophied, with some degree of fibrosis also, a benign stenosis occurs; the orifice may be narrowed by scars of ulcers, or by cancerous new growths. The dilatation may

carry the greater curvature downward, even as far as the pubic arch, while the smaller remains about normally placed, or the latter may also descend; in this case the change in the position of the stomach is most marked — it may lie almost perpendicularly, the pylorus in the right iliac fossa or even in the pelvis. When slowly developed a hypertrophy of the muscular coat usually coexists; sooner or later, however, the distention mechanically thins the stomach wall and atrophy hastens the change. A form of dilatation from traction occurs, but seldom reaches so marked a degree, when the omentum is included in a hernia and constantly pulls on the greater curvature, or when the transverse colon is constantly loaded with feces in the habitually constipated, and also exerts a downward traction. When stenosis is the cause the dilatation may be called mechanical; when loss of tone and obscure nervous influences, together with atrophy of the muscular layers, cause the distention, it is termed dynamic. Stenosis occurs after cicatricial contraction of large sections of the stomach wall and from starvation. When the suspensory ligaments of the liver and other viscera become stretched and a general enteroptosis occurs, the stomach as a whole may be variously dislocated.

**Foreign Bodies** of all kinds are swallowed by the hysterical and insane. Intestinal parasites occasionally make their way into the stomach, as round worms and tenia, and may be vomited. The contents of the stomach at autopsy may be food or medicine or small amounts of mucus, or chemicals taken by accident or with suicidal intent; at times in intestinal obstruction, and in the insane from coprophagy, the stomach contains feces.

The microörganisms found in the stomach are yeast cells, sarcina, oïdium albicans in aphthæ, bacillus filiformis (especially with carcinoma), and others connected with fermentative processes.

## The Intestines.

**Malformations.**—Congenital absence and reduplication of parts of the intestinal tract occasionally occur; stenosis is more common and may affect any section of the tract; the colon may end blindly at the sigmoid flexure or the rectum at the anus (*atresia ani*). The rectum also may be one common cavity with the urinary and genital organs (*cloaca* formation). The commonest diverticula arise from the omphalo-mesenteric duct and the flow of intestinal contents may be diverted out through the navel when this false communication is ample, the gut below being stenosed or atresic. Most commonly only a small diverticulum (Meckel's) like the thumb of a glove, is found above the ileo-cecal valve (in the new-born 0.5 meter, in the adult usually about 1.0 meter above), which projects from the convex side of the gut and is empty, its walls being formed as are the intestinal. If very long it may strangle part of the intestine or foreign bodies in it may lead to perforation.

*Hernia.*—Among variations in the location of the gut partial dislocations as herniæ may be mentioned. These are protrusions of the abdominal contents through some weakened or deficient portion of the enclosing walls, and they may be congenital or acquired. If the hernial sac lies without the abdomen it is called an external hernia, if the hernia passes through the diaphragm or into the retroperitoneal tissue it forms an internal hernia. The contents of the sac may include almost any one of the abdominal organs or be limited to a portion of the small intestine. The mechanism of all hernias may be referred to one of three causes, either increase of the intra-abdominal pressure in combination with a weak place in the wall, or abnormal length of the mesentery with the above, or masses of fatty tissue localized in the subperitoneal layer which mechanically or by atrophy increase the spaces between the fibrous elements, so that a pocket might possibly form into

which abdominal contents might be pushed. Practically the only cause requiring consideration is the first, combined pressure and a weak wall, and certain parts of the wall are very liable to give way before the pressure of coughing, crying and muscular effort, especially lifting heavy weights. These are the inguinal and femoral rings, the neighborhood of the umbilicus, and parts of the diaphragm when imperfectly developed. Hernias through the sciatic foramen, the fibers of the levator ani, the obturator foramen, and Douglas' pouch into the vagina have been described, but are very uncommon.

The contents of the hernial sac, being exposed to circulatory disorders on account of the stretching and twisting of its vessels which may follow, are liable to various chronic inflammations which form adhesions between them; acute inflammation may occur after injury. Compression of the veins leads to stasis, thrombosis and gangrene; when the arteries also are compressed it leads to rapid edema, inflammation, hemorrhage and gangrene. Hernias which may be pushed back through the opening or ring by which they escape are called reducible; if adhesions or other cause prevent this they are called irreducible; when the neck of the sac is tight and stasis occurs the hernia is said to be strangulated. This strangulation may occur because of the small size of the ring, because intestinal onflow or internal edema increases the size of the sac's contents, and hence the pressure on enclosing parts, or because other abdominal contents force their way in, as a piece of the omentum. If the strangulation is soon relieved and moist heat applied the gut may return to its normal condition. The part most often found in the sac is the small intestine, then the colon, and, with either, part of the omentum.

**Stenosis and Dilatation.**—The contraction of fibrous tissue after ulceration in the gut, or pressure from without, may narrow its caliber or occlude it; the part above then dilates while the distal portion shrinks and atrophies. Complete occlusion is rapidly fatal; degrees of stenosis not incompatible

with life may cause gaseous distention and intestinal dyspepsia, with constipation. When the gut is twisted on its long axis, which may occur in any part not too firmly attached, and which is favored by a long mesentery, *volvulus* occurs. A second kind of volvulus occurs when a triangle of the mesentery, with a coil of the gut along its outer arc, twists about its apex, at the vertebral attachment. In either case, stagnation of the intestinal flow dilates the upper portion and the circulation being more or less completely stopped, thrombosis, with consequent edema and gangrene, is easily produced; above the constriction the gut may ulcerate and perforation occur. Adhesions between coils of the intestine in very favorable cases may allow perforation of adjacent walls. This reconstitutes the intestinal lumen and relieves the stasis in its contents; otherwise, fatal peritonitis is most probable.

When a portion of the intestine is received within the lumen of a portion below it, *intussusception* or *invagination* occurs, the receiving part being called the *intussuscipiens* and the swallowed portion the *intussusceptum.* The length of the latter may be a few cm., or the major portion of the gut above the site of the invagination; it grows by steady ascent of the receiving portion, so that what was the apex of the intusscep-tum remains the apex however long it becomes. The inner portion may undergo a second intussusception, or several such places may be found along the course of the gut. Such a multiple invagination occurs in infants during the death agony at times and is without significance as a cause of death. When an invagination is formed it is almost always in the direction of the intestinal flow, the upper part being received into the lower, and its origin, while obscure, may be in convulsive peristalsis; in rare cases reverse peristalsis occasions an invagination in the other direction. Because of the tension and twisting of the mesentery of the intussusceptum circulatory disorders immediately follow, with edema and stasis inside and inflammation without; the result of the inflammation is to bind the

peritoneal surfaces together and make the dislocation irreducible. The part most often invaginated in adults is the lower end of the ileum with the head of the colon into the colon, the ileum in children passes into the cecum or the descending colon into the sigmoid portion. The end of the process varies with the degree of disturbance in the blood supply and of stenosis in the gut. It may become permanent, with the fluid contents of the gut passing fairly well; the intussuscepted portion may slough into the canal and be carried away, with nearly complete cure of the condition; or fecal obstruction may be complete and death rapidly follows; or perforation may set up a fatal peritonitis. Some cases appear to result from polypoid tumors within the intestine, which, by peristalsis, drag on a portion of the wall and invert it; others occur with large masses of imperfectly digested food in the intestine, and probably irregular peristalsis; many others can not be explained.

The rectum is liable to prolapse when its walls are dilated and loosely attached and when the sphincter is weakened; it usually occurs with violent efforts of defecation and when the prolapsed gut is replaced it is very apt to protrude again. If left unreduced it may become inflamed acutely, or even gangrenous, the sphincter strangulating it more or less, or a chronic thickening is observed and the mucous surface is apt to be ulcerated in places.

**Perforation and Rupture.**—The intestine may be opened by perforating wounds, stabs and bullets most commonly, or by ulcerative processes from within. If the perforation is small it may be closed by fibrin and healed, if larger the intestinal contents usually escape into the peritoneum and cause fatal inflammation. When the perforation has occurred slowly, as in tubercular ulcers of the gut, fibrinous adhesions may prevent the escape of feces for long periods, and in some cases the ulcerative process opens through the abdominal walls and a fecal fistula is the result. Rupture of the intestine may

follow contusions of the abdominal wall or enormous accumulation of gas in the canal. The most frequent place for ulceration and rupture is the appendix vermiformis, that is, apart from typhoid and other ulcers.

**Disorders of Circulation.**—*Anemia* of the intestine occurs in starvation and other cachexias and after severe hemorrhage. *Acute congestion* may be localized about the lymphoid follicles or in scattered areas or diffuse, and the serous surface may share in it. *Passive congestion* is a common result of obstacle to the portal flow, as in cirrhosis and tumors of the liver, and to a less marked extent follows lung and heart disease with impeded venous return. In this case the veins of the gut and the mesentery are swollen and prominent, and a special line of varicosities sometimes develops along the reflection of the peritoneum from viscera to wall in long-standing liver disease with portal stasis.

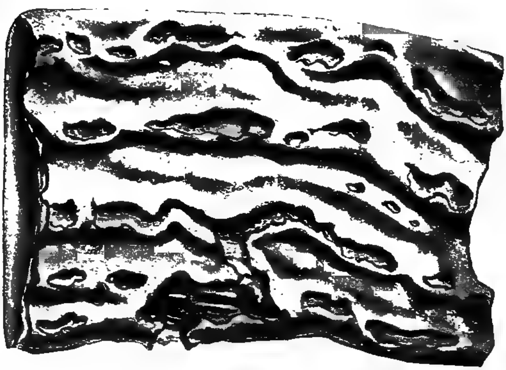
Submucous *hemorrhages*, as little points, occur in the upper part of the small intestine with severe congestion and in hemorrhagic constitutional conditions. Larger bleeding into the canal may follow ulceration, chemical corrosion, and wounds, as the bites of parasites, but sometimes it occurs without apparent cause. Perhaps the commonest ulcer to cause intestinal hemorrhage is the typhoid.

*Edema* of the intestinal wall may be most marked on the mucous surface or general throughout the wall; it occurs with venous stasis, acute inflammations, and especially in specific inflammations as from anthrax infection. Embolism may produce infarcts but usually the profuse anastomoses between the vessels relieve the part. Certain forms of ulcer may depend upon such embolism and consequent necrosis of the mucosa (as in the duodenum after superficial burns).

**Inflammation.**—Simple acute inflammation of catarrhal form is common after causes which produce it elsewhere. It may be reflex from chilling of the body, especially of the abdomen and buttocks; and irritants swallowed with food, and parasites,

are common causes. The inflammation may be limited to one portion of the small intestine or involve the whole gut. The follicles are swollen and prominent on a hyperemic mucous membrane, and rapid transudation into the canal, with increased peristalsis, hastens the passage of feces; hence diarrhea is common in even slight grades of this disease. When large masses of epithelium are loosened from the wall and passed in the feces, it is called *desquamative enteritis,* and when fibrin

FIG. 99.



DEEP ULCERS OF THE JEJUNUM, WITH UNDERMINED EDGES, SITUATED ON THE FREE MARGINS OF THE VALVULAE. (*Ribbert.*)

converts sections of this into tubes it is called *croupous enteritis,* a form common with young children. In these severe forms erosion of the mucosa produces a few or many superficial ulcers, usually small and of a yellowish color from purulent infiltration. Sometimes the inflammation specially affects the follicles and very small ulcers remain, which may be lightly pigmented, singly or over large areas.

Chronic inflammation may proceed from an acute attack or repetitions of it, or may be caused by parasites and fermentation in the intestine. Certain slow poisonings, as lead and

mercury and arsenic, regularly produce chronic catarrhal enteritis. The mucosa is thickened, covered with viscid mucus; passive hyperemia may give a cyanotic color to the whole thickness of the wall. Hyperplasia may affect the glands or the fibrous elements, or both, and the gross and microscopic appearances vary accordingly. Atrophy of the glands usually follows, and the site may be marked by pigment of a grayish or black color. The muscular coat may hypertrophy or atrophy. Functionally, constipation, or alternate constipation and diarrhea, with putrefaction of contents and symptoms of absorption of the products of decay — headache, dizziness, foul breath, coated tongue, etc., are the clinical manifestations of chronic enteritis, and the urine contains indican and ethereal sulphates.

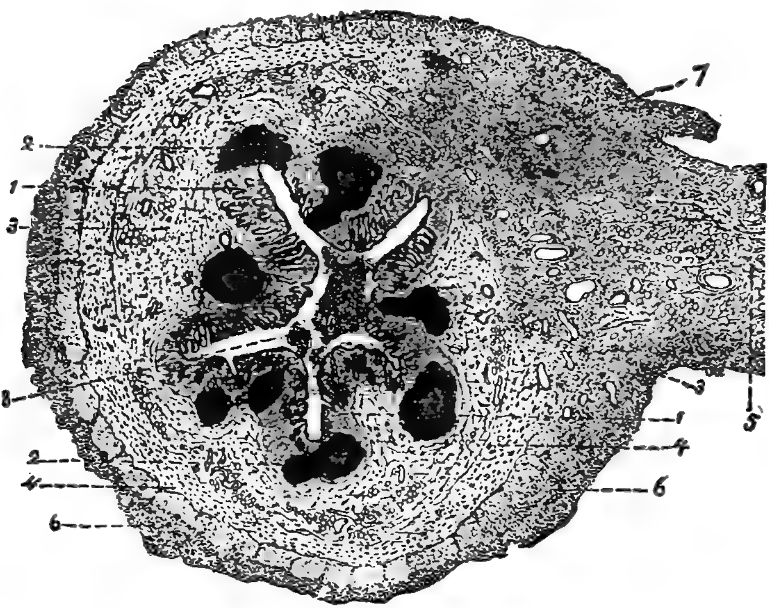
**Degeneration.**—Atrophy and pigmentation have been mentioned. A marked form of the latter occurs in chronic alcoholism, in malaria and anthracosis; the pigment may be found also in the liver and spleen. Amyloid degeneration of marked degree in other organs affects the intestine also; independently it does not seem to occur. The amyloid material is found chiefly in the smaller arteries and capillaries of the villi and connective tissue.

While these characters of inflammation and degeneration are common to the whole tract of intestine, certain portions of it present peculiarities which may be briefly mentioned. *Duodenitis* usually follows gastritis and from the same causes. Because of the entrance of the common bile-duct in this portion, edema and ascending inflammation may close off the flow of bile and pancreatic juice, and hence icterus is a common symptom of duodenal catarrh. The cecum is specially liable to contain masses of feces, because of the mechanical disadvantage under which they pass to the transverse colon. They may set up acute or chronic inflammation or lie passively and collect to enormous masses.

*Appendicitis.*—Th appendix may contain hardened feces, calculi made up of stratified lime salts, foreign bodies as seeds. Be-

cause of its narrow lumen, and large proportion of lymphoid tissue, and liability to hyperemia and edema, constriction of its vessels and acute inflammation readily follow. Slight wounds and necroses in its mucous membrane permit the colon bacillus

FIG. 100.




ACUTE SUPPURATIVE APPENDICITIS. (*Delafield and Prudden.*)

Appendix removed by operation twelve hours after first symptoms. Streptococcus in the exudate. 1, mucosa of appendix; 2, lymphatic nodules in mucosa; 3, submucosa; 4, muscularis; 5, mesentery of appendix; 6, pus and fibrin covering the appendix; 7, dense infiltration of wall with pus.

or other pyogenic bacteria to attack its tissue and set up acute suppuration, and, as in other lymphoid areas (Peyer's patches), phagocytes may introduce the bacteria deeply enough to cause the inflammation. The bacilli and their products cause a round-

celled infiltration with serous exudate; in these inflammatory products as a culture medium they multiply rapidly, and they and their toxins are confined there; the cells of the place break down, polynuclear leucocytes assemble in numbers, and a suppurative focus is established. When the appendix lies behind the colon the resulting abscess lifts this part upward; when it lies free in the peritoneum the adjacent coils of intestine adhere and shut off the inflammatory process from the general cavity. In these ways local collections of pus form, intestinal contents may be added, rupture may occur into the gut or the peritoneum or externally. Fatal peritonitis is the usual result in neglected cases. When the inflammation is less acute and more productive the lumen of the appendix may be obliterated.

*Colitis* may be limited to the cecum, the sigmoid flexure or any other part of the large intestine or involve the whole of it. Acute forms occur as dysentery and may be caused by poisons from without the body (mercury especially) or from within (as in chronic nephritis). Chronic forms are common with habitual constipation and the constitutional results of absorption vary from malaise and chronic headache to severe copremia and death in coma. When the rectum is the seat of the inflammation it is called *proctitis*, acute or chronic, and the former is very apt to pass over into the latter. The pathological appearances do not require special description. One form of chronic colitis is peculiarly resistent and persistent, the form accompanied with croupous casts of the bowel, and masses of thickened mucus, at times passed with much abdominal pain, at others the only constituent of the stools and passed almost without special sensation. With this condition, which may follow acute attacks but quite commonly occurs independently of all ascertainable cause, there are constantly symptoms of nervous debility, headache, complete loss of mental and muscular energy, anemia, and trophoneuroses which suggest that the malady is less a bowel disorder than a nervous functional disease. This is apparently sup-

ported by its occurrence after acute diseases with profound influence on the nervous system, as epidemic influenza. It is very apt to recur after apparent improvement, and mental worry will often bring it on quite suddenly after a previous attack. The ultimate prognosis is not good.

From acute proctitis the neighboring areolar tissue in the ischio-rectal pyramid is at times involved, with abscess formation and perforation into the rectum or through the skin.

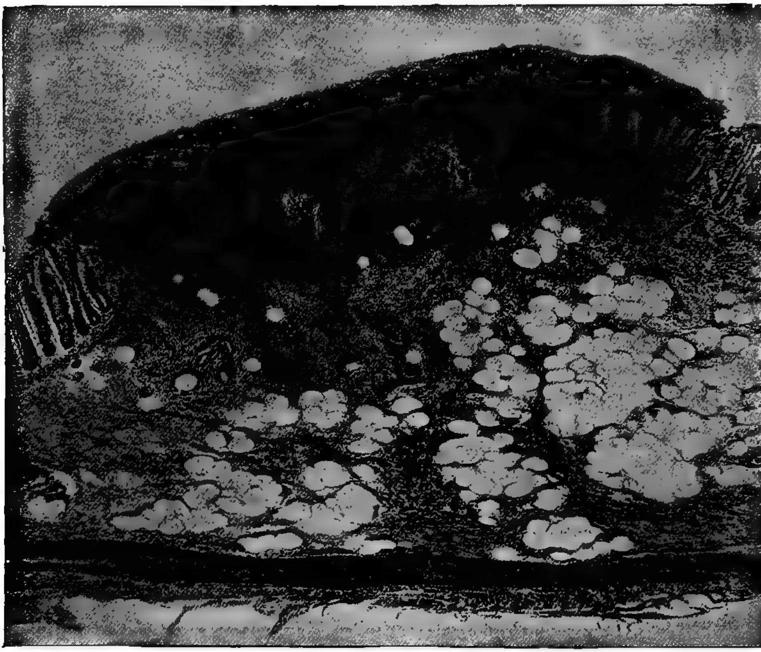
## Enteritis Due to Specific Bacteria.

**Dysentery.**—This term is clinical rather than pathological and covers a number of lesions, which vary from each other, and yet show many transitions from one to the other. The specific organism varies also. It may be an ameba, as in tropical dysentery, invading the mucosa and submucosa, and causing severe ulcerative inflammation; at other times it is the bacillus coli communis which alone, or with b. pyocyaneus and cocci, is capable of producing extensive ulceration here and in other tissues. Still other cases have been described as due to a small bacillus (Ogati's or Shiga's) with rounded ends, actively motile, forming yellow-green colonies on gelatin plates. In other cases, chemical agents, especially mercury, produce ulcers and symptoms identical with dysentery, perhaps by destroying the mucous surface and permitting the bacteria to attack the tissue.

The mucous membrane in the milder cases may show little beyond reddening and edema, with slight increase of secretion, and in more severe only the solitary follicles may be the seat of ulceration. In the most pronounced cases the mucous surface is covered with a false membrane (hence the term diphtheritic enteritis as synonymous with dysentery), and under it the wall of the intestine is sloughing or gangrenous. All variations and combinations of these different grades are encountered. Hence dysentery is sometimes divided into ca-

tarrhal, ulcerative, croupous, diphtheritic, and gangrenous, according as the inflammation is superficial or deep, and the product simple increase of mucus, or fibrin, serum and pus. In the specific disease of the pharynx known as diphtheria, similar

FIG. 101.



NECROTIC COLITIS. (*Delafield and Prudden.*)

Circumscribed congestion and necrosis of glandular and connective tissue coats.

inflammation of any part of the alimentary tract is very unusual, probably due to the destructive action of the gastric juice on bacteria which reach the stomach. Hence diphtheritic colitis refers rather to the coagulation of fibrin in and among the

elements of the mucous surface, associated with necrosis of the same.

In the gross the colon may be covered here and there with a pseudo-membrane, easily stripped off or somewhat adherent, and under it there is a loss of substance constituting an ulcer. The ulcer may have begun in the follicles and remained there or spread; the edges of the folds of mucous membrane are necrotic; at times where the membrane has been removed there are long lines of ulceration. The mucous membrane is generally edematous, and in the early stages the hyperemia may have left hemorrhages in the tissue. The wall of the ulcer is irregular and edematous or necrotic, its base may be the muscular or even the serous layer. The entire colon may present these conditions or limited portions of it, and at times post-mortem changes make parts of it green while others are hyperemic, or gray from the membrane; the whole makes a remarkably variegated appearance. When the ulcers are small and few it is common for them to heal and pigmented scars to remain; even rather large losses of mucous tissue may be replaced in this way.

When the course of the disease has been chronic all varieties of inflammation and ulceration and partial healing may be found in the course of the colon. At times the ulcerating surfaces granulate for long periods and the stools are very purulent. Perforation of the intestine is not common even in severe dysentery. With such profuse ulceration, over such a large surface supplied by the portal vein, purulent thrombi in the veins of the part often occur, pylephlebitis and secondary abscesses of the liver; this is true especially of dysentery due to amebæ, and pulmonary abscess may form in the same way. The ameba may be recovered from the stools or found in the tissue of the intestinal wall and in the secondary abscesses. It is large (20--30 $\mu$ in diameter) and presents a nucleus, vacuoles and inclusions of foreign matter, red cells, pigment, etc. On a warm stage it puts out pseudopods, at first limited to the

ectosarc, then filled with the granular protoplasm; encysted forms occur. These organisms are probably swallowed in drinking water.

**Asiatic Cholera.**—The specific cause of this disease is the cholera vibrio, and its characteristic lesions are produced in the small intestine, although the entire tract may be involved. Post-mortem examination, after death in the stage of asphyxia, demonstrates on the outer or serous surface of the intestines a peculiar mucilaginous film, perhaps more evident to touch than sight. The mucous surface is bright red or bluish in color, with many small submucous hemorrhages.

The contents of the intestine may be copious, thin and watery, and contain small bits of desquamated epithelium, making the so-called rice-water discharge characteristic of the disease. Blood may be mixed with this fluid, rarely a coloring of bile. The rice water fluid is alkaline, has a peculiar stale odor, and contains sodium chloride, carbonate of ammonia and but little albumin (total solid matter from 1 to 2 per cent.).

The mucous membrane is specially swollen in lymphoid follicles, both solitary and agminate, when death occurs early (fourth day). The colon may be slightly hyperemic and edematous, filled with rice-water fluid from the small intestine; at times early in the disease pseudo-membrane forms, and after the algid stage a secondary fibrinous enteritis occurs both in small and large intestine. The stomach may show punctate hemorrhages. The mesenteric nodes are somewhat swollen, firm and bluish or red. The microscopic picture is that of coagulation necrosis and desquamation of the epithelium, confined to the tips of the villi or occupying the entire thickness of the mucosa. In later stages of the disease the intestine may show but little of the rice-water material, bile is usually present, Peyer's patches are pigmented and diphtheritic membranes are found, in the lower part of the ileum especially.

The general appearance of the cadaver is distinguished by tonic convulsion of the flexor muscles, the arms and legs drawn

up and the muscles hard, the hands partly clenched, the face sunken, nose and chin prominent, surface generally cyanotic or only the extremities. Hyperemia of the pia, lobular pneumonia, hyperemia and cloudy swelling in the kidneys, and shrunken liver and spleen are the common associated conditions. The vibrio may be obtained in pure culture from the intestinal mucus and the rice-water contents, and if death has occurred early, sometimes from the gall-bladder; in later stages it may be impossible to find (seldom after the twelfth day).

**Typhoid Fever.**—The characteristic lesion of this disease is found in the lymphoid tissue of the small intestine, especially in the agminate follicles (Peyer's patches), from just above the ileo-cecal valve to 3 meters higher; but occasionally typhoid ulcers occur in the stomach or even the esophagus, more often in the follicles of the colon. In other cases the typhoid infection occurs through the blood or the bile capillaries and the intestinal lesions are not found.

Corresponding to the clinical stages of the disease, divided into weeks, the pathological lesions are so constant that it is fairly safe to estimate the length of the disease from the gross appearance of the intestine. In the first stage the mucous membrane of the lower ileum is actively hyperemic and edematous, the lymphoid follicles moderately swollen, the nearest mesenteric nodes large and very congested. In the second stage the lymphoid structures swell more and more, the general hyperemia may disappear and only the tissue about the glands be red. The Peyer's placques are prominent above the mucous surface on the side opposite the mesenteric attachment, and, as neighboring patches may join, the total length of such a swollen area may be enormous; the lumen of the gut may be lessened by the edema. The surface of the patch is smooth or foveolated, the edge usually sharply defined from the mucous membrane about. The color of these swollen lymph structures is

at first translucent gray, then yellowish from fatty degeneration, afterward dull gray or yellowish as necrosis begins.

Under the microscope the entire thickness of the wall is infiltrated with small round cells and very hyperemic. In the follicular tissue there are also large lymphoid cells with round vesicular nuclei which do not take stains very well; commonly the round-celled infiltration follows the large-celled. Between these the reticulum is at first preserved, afterward it is lost in necrosis.

In favorable cases the process ends here with disappearance of the edematous swelling, with granular and fatty degeneration and resorption of the infiltrating cells. In other cases the edema persists, even increases, the necrotic changes occur in the cellular infiltrate, leading to the formation of a slough which corresponds to the placque in outline, and, when this is cast off, an ulcer is left. Its edges are undermined, its floor is smooth, its main axis is parallel with that of the intestine, it lies opposite the mesenteric attachment and is usually confined to the patch; on the corresponding serous surface there is no fibrinous deposit and perforation is common — all these characters serve to distinguish the typhoid from the tubercular ulcer.

The ulcerative process may be accompanied with bleeding into the canal; if early, from the hyperemia of the mucous membrane and hence not serious, if late, as in the third week, from ulceration of a vessel in the floor of the lesion and possibly fatal. Perforation may occur as early as the end of the second week, during the third, or later, and may lead to general peritonitis or in some cases to a localized inflammation. Occurring without perforation the peritonitis is due to the deep character of the cellular infiltration, great loss of substance when the slough separates, and inflammation of the intestinal aspect of the serous membrane carried through to the other. The mesenteric lymph ganglia usually correspond in their size to the degree of intestinal inflammation, for hyper-

emia, edema, fatty degeneration, suppurative softening or resolution in the nodes usually follow similar changes in the patches. When the ulcers heal both they and the node are apt to be pigmented and this may persist for long periods. The nodes first affected lie in the angle between lower end of ileum and ascending colon; later on those near the root of the mesentery are involved; peritonitis may follow from suppuration in them.

The spleen almost constantly becomes hyperemic and larger and softer; infarct and abscess may occur and the latter set up peritonitis. The muscles of the trunk often show areas of waxy degeneration, especially the recti abdominales, sometimes with hemorrhage; the skin may contain petechial hemorrhages and be necrotic over prominent points; the heart may be the seat of endo- or myocarditis; the blood does not show marked leucocytosis; bronchitis and lobular pneumonia are frequent complications; capillary apoplexies in the cerebral cortex occur; parenchymatous degeneration of the liver is frequent and the gall-bladder contains the typhoid bacilli; the kidney is the seat of degeneration or inflammation, the latter hemorrhagic in some cases, and inflammation and abscess of the parotid gland is found in others; periostitis and osteomyelitis are possible. After the patient is apparently convalescent pulmonary tuberculosis develops in quite a large proportion of the cases.

The typhoid bacilli may be recovered from the affected follicles, the mesenteric nodes, the spleen and the gall-bladder in almost every case; at times they remain for months in the intestine and appear also in the bladder and are voided in the urine; consequently promiscuous urination by typhoid convalescents may be a source of danger to the users of water thus contaminated.

A clinical study of the blood for diagnosis of typhoid fever has been lately introduced under the name of Widal's test or reaction. It depends upon the fact that serum from the blood of one ill with typhoid fever, mixed with a recent culture, will cause the typhoid bacilli to lose their motility and gather in

groups, the whole called "clumping." Three drops of blood are taken from the well-washed aseptic finger tip or lobe of the ear, and each lies by itself on a sterile slide, passed through a flame and cooled just before use; this slide may be wrapped in cotton and transported for examination at the laboratory. Here one drop is mixed with a large drop of sterile water, to redissolve it. A drop from the summit of this is then mixed with six drops of fresh broth culture of the bacillus (not over twenty-four hours old) on a sterile slide. From this a small drop of mingled culture and blood is placed in the middle of a sterile cover-glass, and this is inverted over a sterile hollow-ground slide and examined. The blood received as above or on paper should be diluted with fifty times its bulk to secure the best results. When received fluid, in a capillary tube, a drop may be taken with a fine pipette and nine drops of sterile water added; one drop of this mixture with one drop of broth culture nearly equals 1:20 dilution. A positive reaction is obtained when all the bacilli present gather in one or two masses or clumps, and cease their rapid movement, inside of twenty minutes, and the degree of clumping and time required should always be mentioned in reporting upon the reaction, as also the dilution employed. Sources of error make this test of value, but not entirely reliable. Obtained within forty-eight hours after the onset of a disease the treatment should be as for typhoid until the clinical symptoms demonstrate that the disease is not present. A similar result may be obtained in a macroscopic way by the use of small test tubes and large quantities of the fluids. The tubes are kept at 37° C., and examined for precipitation by a hand lens.

**Anthrax Infection of the Intestine, Mycosis Intestinalis.**—Certain trades which involve handling products of animals liable to anthrax, as wool, hair and bristles, hides and sausage "cases," involve the danger of swallowing dust containing anthrax bacilli or their spores. Infection of the intestine attacks especially the small and upper part of the large,

and appears as areas of a few mm. in diameter up to several cm., on the mucosa of the attached side, prominent above the general surface, brownish-red or ulcerated and yellowish-green, here and there necrotic and of a darker green; from this site they may spread to encircle the intestine. On section marked edema of all the layers is found, the center is purulent and about it is a ring of hemorrhage. The serous coat may be hyperemic over such a place, or generally the rest of the mucosa is often red and swolllen. The mesentery and its nodes are congested and swollen and the peritoneal cavity contains a small amount of serum, at times blood-stained. In some cases the bacilli are found especially in the summits of the valvulæ conniventes, in the gland lumina and the lymphatic channels, or deeper in the submucosa, in the lymph nodes and various organs. The brain and organs where they lodge may show the effects of the bacilli and contain vast numbers in the capillaries. The commonest source of infection is eating with unwashed hands, by which spores are swallowed with the food; bacilli, apart from spores, do not withstand the gastric juice.

**Infectious Granulomata.**—By far the commonest lesion of this variety is *tuberculosis* of the intestine. This may be primary from bacilli swallowed with food, as in milk from tuberculous cows, and hence most often observed in infants. The lymphoid tissues of the lower part of the ileum are especially liable to be affected, caseous and ulcerating foci forming in them and converting part or all of a Peyer's patch into a sluggish ulcer. Secondary infection is common in later stages of pulmonary tuberculosis with copious sputa, doubtless the swallowed bacilli are taken up by phagocytes and deposited in the lymphoid tissue. If a solitary follicle is the seat of the ulcer it appears as a small round loss of tissue with thickened edges and a purulent base. Larger ulcers occupy the agminate areas and at times several become confluent.

As the process follows the lymph channels the inner side of the intestine is girdled by the ulcer, its general outline is oval, it lies with its long axis at right angles to the main intestinal axis unless produced in a placque by junction of several small ones, its edges are thickened and firm because of the fibrous hyperplasia and not undermined, the base is uneven and covered with pus and necrotic tissue, and on the corresponding

FIG. 102.

TUBERCULAR ULCERS OF THE INTESTINE. (*Stengel.*)

Ulcers oval, with long axis transverse, edges thickened and not undermined, bases rough.

serous surface there is an exudation of fibrin, together with little lines and series of tubercles in ring form about the intestine. The ulcer may perforate, but the fibrinous process makes adhesions between neighboring coils or other parts and prevents the escape of fecal matter.

Such large ulcers are not confined to the ileum; they are found as large and in numbers in the colon, and when partly healed, occur as firm scars, often deeply pigmented, alongside

of more recent ulceration. These scars do not narrow the lumen of the gut perceptibly, as do syphilitic processes. The mesenteric lymph nodes are regularly involved and relatively seldom there is general tubercular peritonitis.

*Syphilis* of the intestine is rare, but most common in the rectum in adults; as this is the only portion of the tract exposed to direct infection it is the only site of intestinal chancre. The chronic ulcer developed from gumma of the wall is accompanied by round-celled infiltration and great thickening of the whole wall, papillary projections on the mucous membrane, ulceration and the formation of tough scars which contract and stenose the canal. In the new-born congenital syphilis may affect the duodenum and ileum, the lymphoid tissues being specially attacked.

*Actinomyces* rarely involves the cecum and produces the usual infiltration and ulceration. *Enteromycosis* (*botulinism*) is the name given to intestinal lesions produced by the ingestion of decayed fish, meat and other proteid food, accompanied by catarrhal or fibrinous inflammation and ulceration, profuse diarrhea and constitutional depression. The entire picture is rather that of toxin-poisoning than simple enteritis due to a specific bacterium.

**Tumors.**—Benign new growths may develop from any of the structures of the intestinal wall; myoma, fibroma and glandular polypoid forms, at times combined with lipoma, are the commonest. A form of congenital anomaly occasioned by the constriction of a part of the gut is known as enterocystoma. It usually occurs as a small section of the intestine, atresic at each end and dilated with fluid, by the side of a normally functionating intestine.

Primary sarcoma is unusual, most often round-celled and at times congenital.

*Carcinoma* shows apparent preference for certain parts of the intestine, as the papilla in the duodenum, the ileocecal valve and its neighborhood, the line of junction between the sigmoid and

the rectal portions of the canal. At the anal orifice the tumor may be an epithelioma, elsewhere it starts in the gland follicles (as Lieberkühn's) and soon surrounds the lumen while infiltrating the entire wall. Ulceration of the mucous surface is common, colloid and other degenerations occur oftener in the richly cellular forms, stenosis of the intestine is most marked in the scirrhous. Metastases in the mesenteric nodes and the liver are usually found. (See Pt. I., p. 173.)

**Parasites.**—Among the lower forms amebæ have already been mentioned as a cause of severe dysentery. Balantidium coli, cercomonas and trichomonas are also met with, associated with diarrhea, the cause of it or accidentally present; a better demonstrated relation between infusoria and inflammation occurs with the megastoma entericum. Worms are the most frequent intestinal parasites, and by their presence both local inflammatory and general nutritive and nervous effects are produced. Among the tape-worms tenia solium, mediocanellata and bothriocephalus occur most commonly in man; in Abyssinia a tenia nana is found in almost every person above a certain age and locally considered rather beneficial than otherwise. Nematodes, as round worms, may cause trouble by their great number, running into the hundreds, or by wandering into various lumina, or perforating the wall; for the latter result there is usually an ulcer or other defect necessary. Oxyuris causes chronic inflammation of the rectum in both sexes and wanders into the vagina in females. Trichinæ develop in the gut but do their worst damage in the course of their wandering into distant voluntary muscles. Anchylostoma may cause profound anemia and this is observed in certain countries (Italy, Southeastern United States) more than in others. (Uncinariasis.)

**Foreign bodies** in the intestine may be of any kind which can be swallowed and passed into the canal; or they develop as concretions about some nucleus, as a seed, by successive deposits of lime and magnesium salts; mixed with these are

mucus and bile pigment in varying amounts so that their color is yellowish-white, brown or greenish. These *enteroliths* in lower animals reach a large size (as in ruminants); in man they are commonly small, ovoid, stratified, at times multiple, and of little importance unless wedged into the appendix. Sharp foreign bodies, as needles swallowed by the hysterical, often leave the intestinal tract and wander through the tissues, appearing after long periods under the skin of the thorax or limbs.

The fecal contents may be abnormally hard, forming scybalous masses, from long retention and consequent absorption of their fluid part; or abnormally soft and fluid from the addition of serous fluid, as after hydragogue purgatives and exudative inflammation. The gas normally present may increase to such an extent as to push the diaphragm upward and hinder respiration; this occurs suddenly in certain nervous states and slowly in typhoid and peritonitis. It is called meteorism or tympanites. Connected with it is often a paralysis of the muscular fibers of the intestine and cessation of peristalsis; stenosis of any part leads to much dilatation above it.

# CHAPTER XVII.

## THE ALIMENTARY GLANDS.

### The Salivary Glands.

**Inflammation** of the parotid gland (*parotitis* or mumps) occurs as an infectious disease, characterized by rapid swelling, which may pass to the tissue in the neighborhood and also to the other salivary glands. The inflammation is exudative and chiefly serous in mild cases; when severe, suppuration and abscess formation may follow. Edema may occur in the floor of the mouth when the lingual glands are involved. In adults so-called metastatic inflammation of the testicle and the ovary complicates some cases, and this occurs with the first inflammation or after it disappears.

As a secondary inflammation, parotitis is seen with several general infections, as typhoid and scarlet fevers, pyemia and tuberculosis, and congenital syphilis. The course of the inflammation may be from the larger ducts to the acini, after the former are plugged with exudate. When the tissues about the gland are also involved the swelling and pain become extreme, because so much of the gland is confined behind the angle of the jaw. Such an acute inflammation may disappear and leave no trace, or pass into a chronic fibrosis (induration), or a suppurative stage which forms small abscesses throughout the gland and larger ones by their confluence. Gangrene of the part is occasionally observed in pyemia. At other times the

limits of the gland are passed and the suppuration follows the fascia in the neck, or causes otitis or necrosis of the bones adjacent. The abscess may empty into the mouth or externally and fistulæ may remain. In some of these cases the infection is brought by way of the blood, in others the infection travels up the duct from the mouth.

The submaxillary gland may be involved at the same time with the parotid, or, in very unusual cases, by itself. An extremely severe form of independent inflammation of the submaxillary is known as *angina Ludovici,* and begins as a swelling in the gland, rapid suppuration and extension of the process to the entire suprahyoid region; in later stages it may also travel backward to the larynx and downward into the anterior mediastinum. Abscesses form which break into the mouth or externally, necrosis and gangrene are often associated, and death occurs, in about 50 per cent. of the cases, from edema of the glottis, pneumonia or septic intoxication. This form of angina may start in the submaxillary connective tissue, and perhaps the infection gains entrance through carious teeth, or, as in scarlet fever, it begins in the gland itself.

The sublingual gland may be inflamed by extension from similar processes on the tongue, seldom otherwise.

Hypertrophy of all the salivary glands may follow acute inflammation, when the increase in size is chiefly interstitial, or, as in gum and tobacco chewers, it may result from functional activity long kept up beyond alimentary needs.

**Tumors** of the salivary glands are most often found in the parotid and primary forms are unusual in all. Benign tumors may be fibroma, lipoma, or chondroma, and mixed forms of these occur frequently with sarcoma of the part. Among the forms of sarcoma fibro- and melano- occur; adeno-sarcoma and epithelioma are sometimes found. Primary carcinoma is rare. Commonest among parotid tumors are the mixed forms which develop in children, of slow growth, without metastases (usually), and containing new cartilage, fibrous and sarcomatous

tissue. They reach a large size and mechanically push their way into the pharynx and mouth. They may be explained as fetal inclusions and bear a relation to the outer end of the first branchial cleft.

**The Salivary Ducts.**—Fistulæ remain after abscess opening externally or elsewhere, or after operations which involve incision of the duct. Foreign bodies may make their way into the duct and cause inflammation, and concretions sometimes form here by deposit of mineral salts about a nucleus; these are called sialoliths, and are found both in the main ducts and deeper in. If such a foreign body or concretion causes stenosis of the duct the secretion collects behind it and dilates the part, with pressure atrophy in the acini. Such a retention cyst is called ranula and is most common in Wharton's duct. Another form of ranula begins in a mucous pouch which is occasionally present near the frenum linguæ.

## The Pancreas.

**Malformations.**—The commonest in viable children are accessory lobes of the main gland, accessory glands sometimes with ducts of their own, formation of pancreatic tissue in the intestinal wall (duodenum), and variations in the main duct; this may be double or may open into the common bile-duct or the stomach or in unusual parts of the duodenum. In about sixteen per cent. of all cases there are two pancreatic ducts, of Wirsung and Santorini, opening separately into the duodenum.

**Disorders of Circulation.**—Functionally hyperemia occurs after a meal, relative anemia after digestion ceases, actual anemia in starvation and cachexia. Hemorrhage in and about the pancreas may result from contusion over the site of the gland or from disorganization of the blood. Suppuration may open large vessels and cause fatal hemorrhage, as is sometimes seen in advanced fat necrosis involving the gland.

**Inflammation.**—An acute form with great swelling, hyperemia, and suppuration later, is known as *purulent pancreatitis*. The pus appears in small points through the organ, which may become confluent, or the interstitial tissue is uniformly infiltrated with purulent exudate; such an inflammation may be primary or extend from other organs, and when gastric ulcers perforate the posterior wall of the stomach this form with gangrene sometimes results. Embolic abscesses and a purulent inflammation of the peripancreatic tissue also are observed. Occasionally these cases develop with great suddenness, perhaps most often in men of obese build, and simulate acute intestinal obstruction.

*Chronic interstitial pancreatitis* presents a stage of infiltration, when the gland is larger than normal and somewhat firmer in consistence, followed by a stage of contraction of the fibrous tissue and a noticeably atrophic organ. Alcoholism, syphilis, and ascending inflammation after gall-stones lodge in the ampulla, all seem to be productive of this cirrhotic hardening of the pancreas. The new tissue may begin about the blood-vessels, and as it increases, especially when contracting, the glandular elements degenerate and disappear.

*Tuberculosis* is found in the pancreas, with general infection, as almost microscopic miliary granules in the glandular tissue, or in larger aggregated masses which may soften in the center.

*Syphilis* of the new-born very seldom affects the pancreas, but gummata have been described both in these cases and in acquired syphilis. The fibrosis which occurs in adult life has been mentioned; this at times accompanies similar changes in the liver and from syphilis as one cause. At times congenital syphilis includes such a hardening of the gland.

**Tumors.**—In the obese, as chronic beer drinkers, the pancreas may share in the general lipomatosis of the abdominal organs, usually combined with atrophy or replacement of the functionating epithelium; in late stages but little of the original structure may remain.

Sarcoma is one of the least usual tumors of the pancreas; it may be round-celled or adeno-sarcoma. Secondary sarcomata occur with general spread of the neoplasm.

Carcinoma on the other hand is not uncommon, after similar disease of the gall-bladder, stomach and intestine. Primary carcinoma may occur either in the head of the organ or in other parts, and the hard fibrous forms are most common. If it starts in the wall of the duct the cancer is usually scirrhous, if from the acini it may be alveolar, containing spaces clothed with cubic and polymorphous epithelium in several layers. From the pancreas metastases into the liver, the gall-bladder and the duodenum usually occur. If the tumor is cystic it may be due to retention of secretion and dilatation of the duct, or to degenerative softening within the neoplasm.

**Degeneration.**—Typhoid and yellow fevers, variola and diphtheria, and other infectious diseases are frequently accompanied by granular and fatty degeneration as in the other parenchymatous organs. In the gross the pancreas may be larger than normal, soft and of a dull grayish color, and under the microscope the cells are filled with fine granules or fat. Chronic phosphorus-poisoning causes marked fatty degeneration. It is one of the first organs to undergo post-mortem softening, hence its examination demands caution.

*Necrosis* affects scattered areas of the organ or large sections, and the causes in the two cases may differ. When a large portion is necrotic it may be from inflammation near by which has extended to invade the gland, as with gastric ulcer. In other cases a peripancreatitis leads to partial or entire death of the organ. In others a post-mortem self-digestion simulates extensive necrosis.

When the flow of secretion from the gland is interfered with by contraction or obliteration of the duct of Wirsung (and of Santorini when present), the fluid backs up and dilates the containing channels. If the stenosis is temporary no effect may be produced in the gland, but after a time the epithelial

cells lining the ducts and in the acini may degenerate and be cast off and thus the digestive ferments are able to attack the tissue. The steapsin causes a peculiar form of destruction of the fat, called *fat necrosis,* which appears as small dull gray spots scattered through the fatty tissue; at first these may be found only between the lobes of the gland, and are more frequent than usually stated.

Later the omental fat is attacked and shows the same whitish or gray foci. These are one or two mm. in diameter, clearly marked off from the shiny peritoneum, sometimes gritty under gentle palpation from contained lime salts of fatty acids. The steapsin (or lipase) splits the fat into glycerin and a fatty acid; the latter may unite with alkaline bodies in the tissue. More extensive necrosis, the cause persisting, at times accompanied with purulent exudate, destroys the gland or opens large vessels (veins) and gives rise to bleeding which may be rapidly fatal. The blood may escape into the peritoneal cavity, or it may dissect behind the peritoneum along the sheaths of the psoas muscles into the pelvis, spongy clots and fluid blood filling the artificial cavity. All that remains of the pancreas may be a small portion of the head in the curve of the duodenum and a bit of the tail in the hilum of the spleen; the portion between is converted into a mass of necrotic tissue and clot. From the nature of the process there are no clinical symptoms for a long time and the course of the disease can not be estimated. Microscopically the small areas at the beginning show hyaline places which were occupied by fat cells, fairly preserved cells enclosing fat crystals, calcium compounds with fatty acids which take hematoxylin strongly, and a zone of hemorrhage about all. In subacute cases there may be areas of cystic softening in the omental or other fatty tissue, containing thin puriform fluid and necrotic shreds.

*Amyloid* degeneration occurs as spots and streaks, of dull gray color and firm feel, on the cut surface of the organ; it is found with other amyloid degenerations, seldom alone, and does not

reach so marked a degree as in other organs.

*Pigmentation* occurs in old age, with atrophy and in general deposit in other organs, from similar causes. There is seldom any iron in the pigment.

*Atrophy* may be simple as in cachexia and senility, or associated with replacement of gland by fatty tissue.

Some of these forms of degeneration may be observed after death from diabetes, and experimental removal of the gland in dogs causes glycosuria, which in most cases is rapidly fatal. If is supposed that the islands of Langerhans, which in the human organ lie almost exclusively in the tail of the gland, have a peculiar function in regulating the metabolism of sugar, and that when degenerative changes in the pancreas are accompanied by glycosuria it is because that section is involved where these cell accumulations are found. Extensive lesions may involve the head of the pancreas, without glycosuria, owing to this anatomical arrangement. When the islands are involved the lesion may be a hyaline change in the epithelial elements, or partial, or complete atrophy of entire islands. The well-established fact that diabetes is often accompanied by lesions in and about the fourth ventricle prevents our ascribing all cases to pancreatic disease. The pancreatic lesion is not always of one kind, even in the pancreatic form of diabetes, but certain ones have been found both in obese and cachectic patients.

The duct of the pancreas presents about the same anomalies and diseases, concretions and stenoses, as do those of the parotid and other salivary glands; even a form of pancreatic ranula has been described. Catarrhal inflammation of the crypts of the gland may result in multiple cystic tumors all through the organ, very small and with clear or purulent contents; the latter may thicken and become caseous.

## The Liver.

**Malformations.**—The organ may be entirely lacking in extreme general malformation; variation in the size and number

of the lobes is common, accessory masses of hepatic tissue may be found in the neighborhood, usually connected with the main organ by pedicles. Complete situs transversus involves transposition of the liver; other changes in location occur in fissures of the diaphragm, hernia, and as an acquired form from external pressure of belts and corsets. The line of greatest pressure usually runs obliquely across the right lobe on the anterior surface and at or below the middle of the vertical height, making a groove where the capsule is much thickened and the balance of the lobe below swollen and indurated; the gall-bladder may be distended. Another form of groove occurs on the superior aspect of the right lobe under the dome of the diaphragm and in some cases may be explained as the result of long-continued dyspnea, irregular and convulsive action of the muscular diaphragm crowding portions of the liver tissue together and making acute-angled furrows between them. These may be as many as five or six, each bounded by round prominent ridges of hepatic tissues, running from before backward and below upward. In other cases these grooves are noted in young children who can not possibly have had dyspnea of such a degree as to cause them. In the former case the furrows do not lodge specially strong bands of muscle, in the congenital form they usually do and hence are broader and shallower. The gall-bladder is sometimes lacking; the common duct may open into the stomach. Among other acquired changes in the location of the liver may be mentioned looseness of the ligaments, which permits the organ to fall, downward dislocation from fluid in the right pleura, misplacement connected with kyphosis and other spinal curvatures, and the rotation upward about a transverse axis caused by ascites, pregnancy and tumors in the abdomen.

**Disorders of Circulation.**—The liver resembles the lung in developing as a bud from the alimentary tract and in having two circulations, one for its stroma, relatively unimportant, and one for its function of far greater capacity and importance,

with but little communication between them, and lymphatics to correspond. The portal system is the largest element in the hepatic circulation, contains blood which has already passed the capillaries of the other abdominal organs, and hence is characterized by slow flow of its blood under but little pressure. To this the rapid increase of its total capacity within the organ, due to the division of the main trunk into many smaller ones and these into thousands of large capillaries, of course contributes. Consequently very slight degrees of hindrance to the exit of blood by the hepatic vein causes marked general passive hyperemia of the liver. Pigment, parasites and bacteria derived from the portal territory are almost constantly deposited in the organ.

*Anemia* plays but little part in the pathology of the liver; it may occur locally from pressure of tumors or generally after loss of blood. The gross appearance depends in part on the lack of blood but even more on the proportion of contained fat, bile and pigment. It is pale with a tint of yellow, green or brown, with increased firmness and diminished size; the gall-bladder may be empty or contain a little thickened bile.

*Active hyperemia* occurs locally about inflammatory areas, tumors and wounds; in certain infectious diseases, as typhoid and malarial fevers and hepatitis, it may be general. The organ is swollen, of bright or darker red, soft and friable, and on section blood flows freely. Such a liver begins to decompose soon after death in favoring circumstances and the large veins may contain froth from the presence of bac. aërogenes capsulatus.

*Passive Congestion.*— The underlying cause in the great majority of cases is interference with the blood flow through the hepatic vein. This may be direct, from pressure upon it or the vena cava inferior, as by right-sided pleurisy with effusion which pushes the heart to the left and drags on the vena cava; or it may be indirect and due to mechanical obstacles to the emptying of the right cavities of the heart, as in emphysema,

pneumonia, valvular disease and aneurysm. The common result of such mechanical conditions is dilatation of the central vein in each acinus, then of the capillaries immediately connected with it. Owing to the steady pressure thus exerted upon the liver cells they atrophy, at first about the central vein, in long-standing cases even to the periphery.

On section such a liver shows dark red points and figures, like letters and portions of letters, due to the unequal division of the central veins by the knife. By slant illumination these dilated vessels are seen to occupy slight depressions due to the atrophy of adjacent cells; further out there is a zone of brownish color owing to the presence of atrophic liver cells containing pigment; along the periphery there is a lighter zone of fat infiltration and bile staining. The total effect is that of dark red marks on a lighter ground and in severe degrees the name "nutmeg liver" is used, from a fancied resemblance to the cut surface of a nutmeg. According as the passive congestion is marked the size of the liver is increased; with atrophy it becomes smaller and firmer; hence the appearances vary with the stage of the condition

*Infarct* of the liver from closure of arterial branches is practically unknown, owing to the rich anastomoses between these vessels. Even large thromboses of the hepatic vein may remain without pronounced effects; but small scattered areas of necrosis may be due to embolism in the hepatic capillaries of the portal vein. Similar focal necroses occur in puerperal fever, septicemia from lesions in the portal territory, and arsenic-poisoning. These may be anemic or hemorrhagic, the former appearing as circumscribed points of pale yellow color throughout the organ, with hyaline thrombi in adjacent vessels (capillaries) in many cases. The other form is mixed in color, partly red, from extravasated blood, and partly yellow or paler, from the coagulation necrosis of the liver cells. Such focal necrosis is often most prominent in puerperal diseases.

*Edema* of the liver follows marked and prolonged disturbances in its circulation and is a part of inflammatory processes; microscopically the cells may present vacuoles and the lymph spaces show distention by lymph as elsewhere.

Occasionally, a liver presents under the capsule and through the parenchyma a number of brick or brownish-red irregular markings and spots, due to extravasation of blood and local alteration of the hemoglobin; it is usually the sequel of a chronic process and is to be referred to previous not determinable periods. Other instances of pigmentation are found after chronic malaria, blood disorders with hemolysis, and anthracosis.

**Injuries.**—Wounds of the liver which permit bleeding may be rapidly fatal, though there are instances where apparently severe cuts and stabs were healed. By forcible contusions the organ may be ruptured and the bleeding is usually extreme, the blood collecting under the capsule if this is not torn, or being found free in the abdomen. Such a hematoma is not uncommon in difficult births, especially breech presentations with instrumental delivery. The injury may be a small subcapsular tear, often on the anterior superior surface, or the capsule may be torn and the liver tissue present a ragged single crush or many small wounds; the bleeding comes especially from the thin-walled veins and is usually fatal. Bits of the liver tissue may be forced into the hepatic vein and cause embolism of the lungs, similar to the post-mortem condition of the like nature.

**Inflammation.**—Acute inflammation of the liver may occur with injuries, but most commonly it follows acute disease in the intestinal canal, as dysentery or suppurative processes, and appears as a single large abscess or as many small ones. The usual seat of the abscess is the right lobe and its size may be very large. The first step is a necrosis of the liver cells, granular degeneration with loss of nuclei, with an infiltration of small round cells from the interlobular and intralobular capillaries. Pus cells come later, in the vessels and then free in the tissue, and with their increase a focus of suppuration is formed; by

pressure on the liver cells this induces a degenerative change, and thus increases in size, rapidly or in a slow chronic manner. The pus is usually thick and more or less tinged with bile. The result may be rupture into the abdomen, or through the abdominal wall after adhesions form, or into the thorax, or formation of a capsule and desiccation of the pus with calcareous deposit.

Suppurative phlebitis of the portal vein (pylephlebitis) causes another variety of hepatic abscess, the organ then being filled with dilated channels containing pus, with purulent reaction about them. Abscess at times occurs with parasites or from gastric ulcer, and in pyemia, with suppurative foci at distant points, the pyogenic cocci often accumulate in the liver capillaries and cause multiple secondary abscesses. In any case the hepatic tissue about the collection of pus presents a zone of intense congestion or even hemorrhage, with beginning fibrous hyperplasia if chronic, and in the acute cases all the liver cells may be in a condition of granular or fatty degeneration.

The microörganisms found may be cocci, especially streptococci, bacillus coli, various forms from the intestine and amebæ in tropical dysentery; in chronic cases the pus may be apparently sterile.

Chronic inflammation of the liver is productive and in slight degrees occurs as an induration with chronic stasis, but as a clinical entity it is described as cirrhosis of various forms; these are similar in histology but their gross appearances and clinical symptoms differ.

**Cirrhosis.**—The two chief forms recognized are the hypertrophic, and the atrophic.

*Hypertrophic cirrhosis* is also called *hepatogenous,* the irritant which causes the disease being supposed to arise in the liver, and *biliary* from the icterus and hyperplasia of the bile-ducts. In the gross the organ is enlarged in all its dimensions, the sharp anterior edge is rounded and the weight may be as high as 4--4.5 kilos. On section it resists the knife, but less than in the atrophic form, and the cut surface is mottled with green,

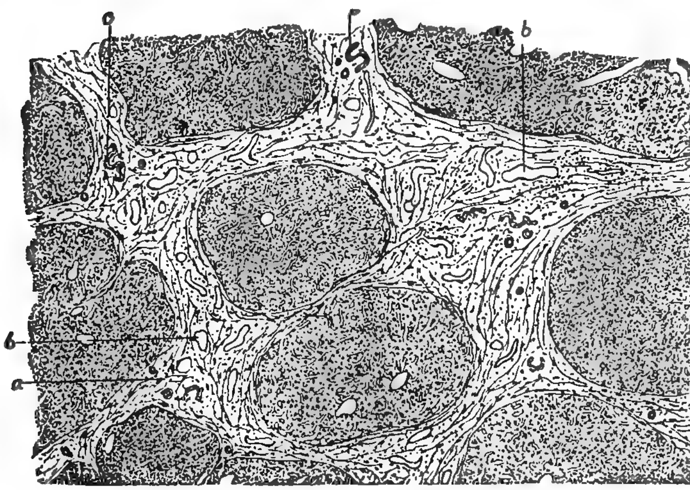
yellow and brown in varying proportions. Close inspection reveals the newly formed fibrous tissue along the line of the portal capillaries and the bile-ducts quite uniformly disseminated throughout, and by the contraction of this the little islands of cells, more or less stained, become slightly prominent on the section. This arrangement has given the name "unilobular" as a synonym, since the acini are involved one at a time, as distinguished from the atrophic form where the fibrous tissue surrounds many lobules and hence "multilobular" is the term employed. Both the surface of the liver and the cut section in this form are smooth, and there is no reason to suppose that a smooth hypertrophic liver ever becomes one of the nodulated atrophic form. The gall-bladder may be contracted but usually contains thin bile and the larger ducts are patent. The lymph nodes in the transverse fissure may be enlarged.

Microscopically the bile-ducts show two changes — they are increased in number and caliber, and many of them are plugged with pigment and cell detritus; about most of them there is an evident proliferation of fibrous tissue, which suggests that the lesion is essentially a pericholangitis. Many bacterial forms have been recovered from such livers and are probably the exciting cause of the lesion. The fibrous tissue may be traced far into the acini between the liver cells as is not often the case in the atrophic form Here and there a hyperplasia of the liver cells may be found but in the main there is marked atrophy and pigmentation of them. In the late stages the bile-ducts show dilatation, hyperplasia of atypical lining epithelia, adenomatous grouping, and suggest transitional forms between cholangitic hyperplasia and primary carcinoma starting in the biliary epithelium.

*Atrophic cirrhosis,* known also as gin-drinker's liver, is sometimes described as hematogenous on the hypothesis that the causal irritation is brought to the liver through the blood, and in the majority of cases this is considered to be alcohol ingested

with food and carried through the portal vein. Beverages with a large per cent. of alcohol, taken into an empty stomach, are specially liable to cause atrophic cirrhosis. It is supposed that the poisonous element in the alcohol is a volatile oily aromatic body known as furfural ($C_5H_4O_2$) which occurs as an impurity in almost all distilled liquors, hence the use of wine or

FIG. 103.




ATROPHIC CIRRHOSIS OF THE LIVER. (*Delafield and Prudden.*)

*a*, new formed connective tissue; *b*, dilated blood-vessels of the new tissue; *c*, gall-duct.

beer does not commonly cause hepatic cirrhosis. Other cases may be due to long-continued intestinal dyspepsia, and consequent irritation of the liver by putrefactive products.

In a well-marked case the liver is smaller than normal and presents both marked induration and shrinking, the new connective tissue being disposed in large bands which run in

various directions and by their contraction divide the organ into many irregular lobes. When these latter are small they project above the surface and resemble nail heads, hence the name "hob-nail" liver, sometimes applied. Owing to the arrangement of the fibrous bands the condition is sometimes called "multilobular," since many acini at a time are grouped and constricted by it. The liver tissue, sharply circumscribed, presents a yellow color if fatty, and with admixture of bile pigment may be darker. The capsule may be thickened or adherent to the diaphragm, the gall-bladder presents no constant appearance except that it is often empty. Adhesions form between the abdominal walls and contents and tend to relieve the portal stasis for a time.

Microscopically the formation of connective tissue may be traced in all its stages in the line of the portal subdivisions, in the youngest places appearing as a focus of round cells about the sheath of the veins with later development of spindle cells. These foci blend and the fibrous tissue becomes poor in cells and firmer, coincident with contraction. This causes compression of the portal capillaries and at the same time there is often an obliterating endophlebitis; the result is to offer an obstacle to the entrance of the portal blood, with increasing stasis throughout the origins of the system. This explains many of the clinical symptoms, the ascites, gastric and intestinal catarrh and hemorrhage, piles, and distention of superficial abdominal veins (caput medusæ), to which latter effect ascitic distention adds. Jaundice, however, appears late if at all and the spleen is not swollen till toward the end. In the hypertrophic form jaundice appears early and is a marked symptom, the spleen is enlarged from the first and the gastric and intestinal hemorrhages seldom occur. In other words the portal circulation suffers especially in the atrophic form and the bile-ducts in the hypertrophic.

A resumé of these two forms will assist in distinguishing them:

| | Cirrhosis. | |
|---|---|---|
| Synonyms. | Charcot's, Hypertrophic, Unilobular, Hepatogenous, Biliary, | Laennec's, Atrophic, Multilobular, Hematogenous, Hob-nail liver. |
| Jaundice. | Early and marked, bile often absent from feces. | Late and slight, bile usually present. |
| Ascites. | Late and unimportant. | May be early; otten enormous. |
| Spleen. | Enlarged early and markedly. | Late and less. |
| Alimentary hemorrhage, piles. | Not common. | Common. |
| Liver. | Large, smooth, mottled, green. | Small, rough, pale or yellow. |
| New fibrous tissue. | In fine lines and strands between acini and cells, involving all parts equally. | In broad bands, making prominent islands in which the single acinus may appear nearly normal; distributed irregularly. |

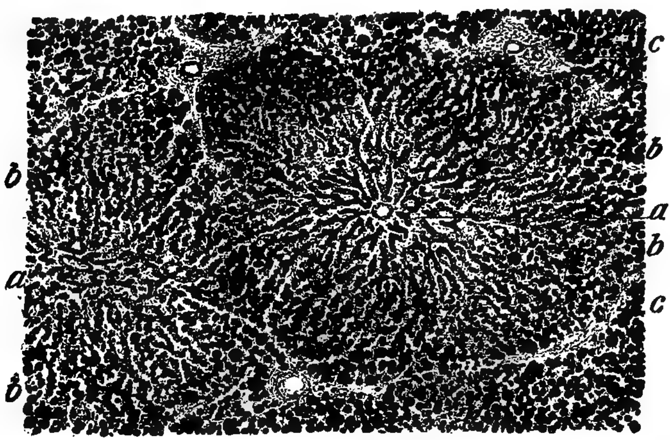
Other forms of cirrhosis have been described, a "paludic" in chronic malarial pigmentation of the organ, an "anthracotic" when pigment taken in through the lungs gains access to the liver and acts as an irritant, and as a complication of diabetes and with great thickening of the capsule (perihepatitis). The essential feature in all is the formation of new fibrous tissue in either of the two ways described above.

When the main bile-ducts are compressed or obliterated the biliary stasis which results, with disorganization of the bile, causes minute peripheral foci of necrosis in the liver and a hyperemia about them. In these foci new fibrous tissue begins to develop and a form of cirrhosis may result which belongs to the "biliary" group, in which the irritant exerts its influence from the bile-capillaries. If pyogenic organisms gain an entrance from the gut before the chronic productive inflammation occurs, the result is suppurative pylephlebitis and multiple hepatic abscesses. The liver in biliary cirrhosis of this variety differs from the hypertrophic form in being smaller, with less pigmentation

and general icterus, and in shrinking with the progress of the disease. (See Syphilis, p. 504.)

**Degenerative Changes in the Liver.**—*Simple atrophy* of the liver occurs with starvation and cachexia of many kinds, the organ being small, its glycogen lost (normally about 3 per cent.), its cells fatty or shrivelled. In a localized form such atrophy follows pressure if exerted for a long time, and more generally it is a senile change. In the atrophic liver there is often an excess of pigment derived from the blood and containing iron.

FIG. 104.




FATTY LIVER. (*Ziegler.*)

*a*, central portions of acini; *b*, peripheral fatty zone; the fat appears black; *c*, interlobular connective tissue.

*Acute yellow atrophy* is a rare disease accompanied by symptoms which suggest infection by bacteria, namely, high fever, jaundice, stupor and convulsions, hematemesis and bleeding from the bowel, the changes in the liver being rapid disappearance of the hepatic cells, softening and yellow hue of the entire organ. In the gross the separate acini can not be made out, the liver is smaller than normal, it is bright yellow or streaked

with red or brown or uniformly of dark yellow brown hue, the capsule is wrinkled and the vessels contain a little thin fluid blood. When bile is present in the gall-bladder it also is very thin and pale. To this combination of pernicious clinical character and hepatic changes the name acute yellow atrophy is given, and its septic nature is evident from the association of the disease with puerperal and other severe infectious invasions. In other cases it is part of a rapidly fatal syphilis or follows extreme icterus, and it occurs also by itself without apparent cause. Many varieties of microörganisms have been found in the bile passage, and the liver substances but none has been proved to be the cause. The above is the usual appearance in rapidly fatal cases, but at times the liver exhibits areas of red or hemorrhagic appearance, where vessels alone are left, alternating with yellow portions, or the bulk of the organ may be of the former color with but small foci of yellow.

Microscopically the yellow parts contain swollen bile-stained cells filled with granules or fat drops, or they are converted into detritus and bile crystals. If this material is absorbed the part decreases in size and all that remains are the blood-vessels, often impervious, mingled with grains of pigment; these are the older and redder portions, in which also there may be remains of hemorrhages.

*Fatty liver* occurs in two forms, which in their most marked development may not be distinguished by the naked eye and yet are radically different in origin and importance.

*Fatty Infiltration.*—The fat normally present in the liver after a meal is a physiological fatty infiltration and appears most clearly in the peripheries of the acini; if the supply of oxygen is good and the function of the organ normal it is transformed and removed. When the supply of fat is relatively large or its combustion imperfect this fatty infiltration of the peripheries of the acini reaches a higher degree. Such a condition may coexist with general emaciation, as in the tuberculous who live on milk, cream, eggs, cod-liver oil, etc., but

attains its most marked development in the case of the chronic beer-drinker, where the weight of the liver may reach twice its normal (3--3.5 kilos).

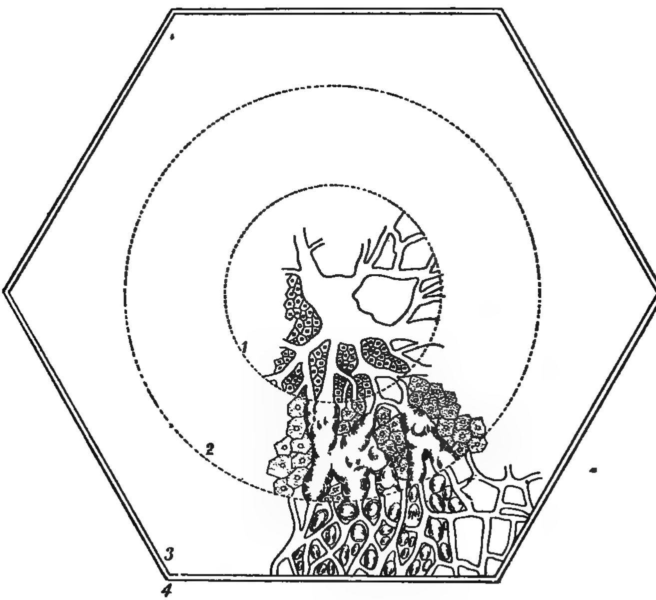
The organ is large, its edges are rounded, it is of a uniform yellow color, slight pressure leaves a dent in it, the knife becomes smeared with fat on cutting into it, and it may even float in water and burn freely when held in a flame. If not excessive the fat will be found in the outer zone of each acinus and on dissolving it out with ether the cell with its nucleus will be found; with dilated central veins the nutmeg liver is formed. In later stages all gross distinctions are lost in the uniform buttery mass and the cells have many of them suffered in nutrition, partly because the organ is anemic from the pressure exerted on the blood-vessels.

In *fatty degeneration* the liver is usually smaller than normal yellowish, friable, and on microscopic examination the fat occurs in smaller droplets in the cells, which are also the seat of albuminous degeneration. The fat is found disseminated through the organ, not confined to the peripheries of acini, and other organs show similar degenerations, the whole being part of general diseases like pernicious anemia, variola, pyemia, yellow fever, etc. The distinction is easily made with teased preparations even without reference to other organs. Severe fatty degeneration occurs with phosphorus-poisoning.

*Amyloid Degeneration.*— As elsewhere this change follows long-continued cachexia, suppuration, tuberculosis, and is associated with similar degeneration of other organs. It has its seat in the walls of the vessels, the hepatic artery, its capillaries, and the portal branches, but in the case of man does not attack the hepatic cell. When pronounced the liver is large, its borders are rounded, it is firm, inelastic, and on section of a pale and dull yellow or a brownish or grayish-red. The middle zones of the acini are the first affected, and the hepatic cells undergo atrophic and degenerative changes from pressure

combined with lessened nutrition. The walls of the vessels involved are converted into dull and swollen strands in which no lumen may be found.

FIG. 105.




PATHOLOGICAL ZONES IN THE HEPATIC ACINUS.

Diagram of a lobule as a six-sided prism, cut transversely, entirely surrounded by fibrous tissue (this is not the case in the normal human liver). 1, circle of dilated central vein (passive congestion), stasis, and pressure atrophy; vein appears dark red and slightly depressed; 2, zone of amyloid degeneration, the vessels converted into swollen masses of amyloid, waxy in the gross; 3, zone of fat infiltration; appears light yellow in the gross; 4, line of connective tissue increase, pale and gray on fresh section. All these limits are exceeded in advanced lesions.

**Infectious Granulomata.**—*Tuberculosis* of the liver is secondary to infection of other organs or part of a general miliary disease, and appears either as miliary tubercles, sometimes

almost invisible to the naked eye, or larger forms with a zone of inflammatory reaction, or old caseous foci. In the chronic forms, which often follow tubercular peritonitis, cirrhotic fibrosis is common.

*Leprosy* produces nodules in the liver, as in the spleen, which start in the connective tissue of the organ and contain the bacilli, as do the capillaries of the part.

*Syphilis* is the most important of the granulomata found in the liver and occurs as disseminated cirrhotic inflammation or as localized gummata. In the cirrhotic form (hepar lobatum) the liver is variously distorted and divided into lobes by scar-like bands. These may nearly divide a portion of the organ from the rest, and the irregular disposition of the new tissue distinguishes it from atrophic cirrhosis, of the alcoholic type. Early stages of the lesion are seldom encountered, but probably the process begins as a gummous inflammation about the branches of the portal vein and the main gall-ducts, with increased size of the organ and thickening of the capsule.

Gumma occurs as localized lesions, from a few millimeters to several centimeters in diameter, and also in combinations with the former lesion. The centers of the larger nodes may be caseous and about them, especially when recent, there is a zone of hyperemia. Microscopically giant cells occur, less freely than in tubercles, many eosinophile cells, necrotic liver cells, and spindle cells peripherally. In the older foci the necrotic process leaves nothing distinguishable but a fibrillary stroma filled with cell detritus.

Congenital syphilis affects the liver in diffuse forms and as gumma, and also as miliary points throughout the liver or gathered in groups resembling tubercles, and in the majority of cases seems to begin in the portal capillaries and is associated with pulmonary syphilis. In an acute form, with severe fatty degeneration, the so-called acute yellow atrophy of the liver in the new-born has been described though it is really congenital syphilis of the organ.

Lymphoma of the liver occurs at times with acute diseases, such as typhoid and variola, and is regularly found in leukemias.

**Tumors.**—True hypertrophy of the liver is most unusual except as partial compensation of one part when another has been destroyed.

Primary tumors of all kinds are not common. The benign include fibroma and lipoma, and, more often, angioma of the cavernous form, which may reach a large size.

*Sarcoma* is at times primary in young children and several varieties have been described. Secondary tumors of this kind occur with sarcoma of the kidney, testicle, bones and eye (often melanotic), and, as in the case of secondary carcinoma, are at times due to transfer of microscopic masses of neoplasm and embolism of portal capillaries.

*Adenoma* occurs in nodules of a reddish or grayish color or diffusely, or in combination of these two. When a cirrhosis coexists the gross appearance resembles that of carcinoma, and even microscopically there is difficulty in distinguishing them at times. A form still more uncommon is the *hypernephroma* which develops from portions of adrenal tissue included in the liver during fetal life. In site they usually correspond to the right adrenal and are apt to be encapsuled; they may be pure or enclose also hepatic cells and gall-ducts.

Primary *carcinoma* of the liver is rare. It occurs as one or more large tumors, or diffusely with increase in the size of the organ and fibrosis, and in an interlobular form which probably arises in the bile-ducts. Perhaps development on a cirrhotic basis is the most common, the gall-duct epithelium being stimulated to hyperplasia instead of degenerating, and leading to adenoma or carcinoma or combinations of these. The characteristic of carcinoma starting in this way is the irregular arrangement of its elements whereas in adenoma a stroma with glandular alveoli, clothed with atypical epithelia but still fairly regular in arrangement, is more common. Other forms appear

to develop from the hepatic cells and present great polymorphism in their epithelioid elements. Fatty and other degenerations, biliary and melanin pigmentation are observed in these tumors. The liver tissue may be atrophic from the pressure, the tumor far exceeding the liver tissue in mass, or it may be hyperplastic in places and degenerated in others. Vast numbers of new-formed bile-ducts occur in some forms, especially where there has been a preceding cirrhosis and new growth of the ducts. Primary carcinoma is perhaps more common in the left lobe than the right, but rare in any case.

Secondary carcinoma follows similar disease of the stomach, pancreas, intestine, kidney and more distant parts. It is most often seen in the right lobe, or in both when observed later in the disease, and may be a few large tumors or many small ones. The larger masses are often umbilicated from softening and absorption of their centers. It frequently corresponds in its distribution to the portal vessels and carcinomatous emboli may be found in them, as well as places where such emboli are invading surrounding tissue.

*Cystic tumors* in the liver are unusual and seldom of any great size; they start in the gall-ducts, perhaps also in lymph channels, and usually contain clear or yellowish fluid.

**Parasites.**—Ameba coli occurs in the liver in tropical dysentery both in the tissue and in abscesses. The psorospermiæ of lower animals (rodents) have been found. Pentastomum denticulatum, the larval form of the dog's p. tenioides, occurring in small cysts, distomum hematobium in the portal veins, distomum lanceolatum (in China and India), and distomum hepaticum of ruminants (sheep), have all been described as occasional inmates of the liver tissues. The most important parasite is perhaps the echinococcus, which occurs in the three forms e. scoliciparиens, being the larval form of the dog's tenia echinococcus, the e. hydatidosus, and e. multilocularis. The results of such cystic growths, which may attain a large size, are partly those of compression, causing icterus and ascites, and partly those due

to rupture, into the peritoneum, the vena cava with general dissemination, and elsewhere. If pyogenic bacteria are present, abscess formation complicates the disease; in other cases the fluid may be absorbed and the site remain as an irregular scar.

## Gall-bladder and Ducts.

**Changes in Caliber.**—Stenosis of the main gall-ducts occurs usually from outside pressure, as by the contractions of inflammatory adhesions, enlarged lymph nodes, various tumors of the liver and adjacent organs. If the cystic duct is closed the other ducts are but little dilated, but the gall-bladder may become much distended by mucous and serous fluid, either bile-stained or clear; this is called dropsy of the gall-bladder. When the hepatic duct is compressed the entire system above the obstacle dilates, even to the fine capillaries, and to this pyogenic infection may be added (suppurative cholangitis). Stenosis of the common duct, usually at its lower end, results in dilatation of all the bile passages and also the gall-bladder, the mucous folds in the common duct are obliterated (valves of Heister), the wall of the duct is thickened and parts of the dilated system may rupture, oftenest the gall-blader. The liver necessarily suffers, if the condition persists, its cells becoming bile-stained, especially in the outer zones of the acini, followed by marked fibrous proliferation along the ducts and cirrhotic contraction of the organ, and at times inflammation of the ducts or areas of necrosis. Of all causes for dilatation of the ducts the commonest is lodgment of gall-stones and this is most frequent in the larger ducts; if they lodge in the ampulla of the common duct they may produce stasis of both the hepatic and the pancreatic excretion.

**Inflammation.**—*Cholangitis* is most evident in the large ducts, corresponding to its usual origin by extension from the stomach and duodenum. It may be simple catarrhal swelling and hyperemia of the lining mucous membrane, and in severe

grades of this disease the ducts may become partially closed by the edema of their walls, resulting in stasis of the bile-current above, dilatation of the bile-ducts and obstructive jaundice. When the edema subsides the gall flows again into the gut, and the condition is relieved. If chronic, the inflammation may produce dilatation of the main ducts and polypoid growths. Other causes of the disease are irritation by gall-stones, entrance of parasites from the intestine, as round worms, and extension from adjacent structures.

Purulent inflammation of the ducts follows injury by gall-stones, abscess formation near by, especially if breaking into the bile-passages, stasis and disorganization of the bile with pyogenic infection from the gut. It complicates certain general diseases, as typhoid, dysentery and pyemia. The mucous lining of the part is then swollen, discolored, and even necrotic, and the ducts contain yellow or bile-stained muco-pus. The inflammation may pass to other structures, favored by anatomical relations, as to the portal vein, causing pylephlebitis, or to the liver tissue, with abscess formation.

The gall-bladder itself may take part in such a suppurative inflammation or remain for a time uninvolved; it may also be the only part inflamed. The cause of such a local inflammation is most often irritation by gall-stones; dilatation of the part is common, by mucous or muco-purulent fluid; ulcers may form in the wall and open into the peritoneum, the stomach or intestine, or through the abdominal wall. The course of the disease is often chronic and interrupted by periods of apparent recovery. When the gall-bladder is distended with pus it is termed *empyema* of the part.

**Cholelithiasis.**—Gall-stones are found in about 7 per cent. of all autopsies, but are far commoner in females than in males. It is probable that they form, like vesical calculi, about a nucleus, which may be bacteria or thickened mucus, less often a foreign body from outside. On this a layer of biliary salts and albumin is deposited, a process favored by stasis of the

bile and partial decomposition of its elements, and successive layers are added till a relatively large size may be reached; or many small stones may form. Mutual attrition usually wears facets on the calculi when few and packed together, giving roughly pyramidal and crystalline shapes to them. In size they vary from grains of sand by the hundred to a single stone as large as the gall-bladder will contain. While usually formed in the gall-bladder they may form elsewhere, as in the larger ducts. The color varies from light yellow through different browns to black, and their chemical composition may be pure cholesterin, or bile pigment, or the two combined, or calcium salts, but most commonly they contain all these elements, and the larger forms are usually in concentric layers.

The results of such formation of biliary calculi may be postponed for years if they lie quietly in the gall-bladder, though there is always a possibility of their causing suppuration, but when they pass into the cystic and common bile-ducts they cause biliary colic, probably the severest pain known, in which death with symptoms of collapse may occur. If not too large to pass into the gut, aided by pressure of accumulated bile above them and gradual slight dilatation of the canal, the escape is proclaimed by sudden cessation of the pain. Such attacks may recur at various periods in the same patient. If they lodge in the course of the outward journey they may cause suppurative inflammation, adhesions, and perforation into the peritoneum or some part of the alimentary canal.

**Tumors.**—As a general statement all benign and sarcomatous tumors are uncommon in the gall-bladder and ducts. Primary carcinoma seems at times to be associated with calculi of the part, though these would probably form in any case from the stagnant bile. In the biliary passages in the liver primary carcinoma may start in the mucous glands of the wall or, after prolonged misdirected hyperplasia, in the epithelia lining the

ducts. A frequent site of the neoplasm is about the lower end of the common duct.

**Icterus.**—A symptom common to many diseases of the liver and its ducts is staining of the organ and of various tissues of the body with biliary pigments. This is known as *jaundice* or *icterus* and is usually described as of two varieties, hematogenous and hepatogenous, as if bile pigment were formed in the circulating blood as well as in the liver. The opinion now is that the only source of bile pigment is the hepatic cells and hence strictly there can be no hematogenous jaundice. And yet there are cases where general yellowness of the tissues occurs with no trace of mechanical obstacle to the flow of bile, as is proved by the presence of bile in the feces during life and no apparent hepatic lesion after death. Such icterus is common in certain infectious diseases, certain intoxications, and occurs in the new-born as icterus neonatorum. It may be produced experimentally by injection of various substances into the blood-vessels of animals, as frozen blood, toluylendiamin, etc.

These cases of icterus may be explained as the result of disordered innervation, for there are dilator fibers from the sympathetic which open the duct, and constrictor fibers from the vagus which close it, and the pressure in the bile ducts is so nearly negative that a very slight loss of balance will prevent the flow, quite apart from inflammatory swelling of the common duct. Access of toxic substances to the liver, and disordered flow of bile formed in the hepatic cell, whereby it reaches the capillaries of the lymph system instead of the biliary, will explain other cases. The name *paracholia* has been given to some cases of icterus, and among them may be grouped those which follow chloroform, phosphorus and serpent poison, pyemia and other infectious diseases, and some cases of icterus neonatorum; though in the latter case mechanical alterations of the circulation in the new-born and edema of the periportal tissues have been supposed to be causal.

Hepatogenous jaundice in the old sense, also called obstructive and resorptive, occurs when there is an obstacle to the flow of bile into the intestine, and the obstacle may be in the papilla, the main ducts, as in catarrhal jaundice, associated with catarrhal inflammation of the duodenum and main ducts, or it may be within the liver from stenosis of the capillaries, inflammation of their walls, and various compressions. Obstruction of the large ducts by inspissated mucus, gall-stones, round worms, echinococcus cysts and pressure from neighboring organs will explain other cases. In some instances thrombosis of the portal vein, loss of motion in the diaphragm and severe emotional crises may cause it.

Since experiments indicate that icterus occurs only so long as the lymphatics of the liver remain patent, all varieties appear to result from a diverted bile circulation; to which dilatation of the bile capillaries directly tends since it loosens the hepatic cells and facilitates entrance of the bile into the perivascular lymph spaces. The liver normally has an internal secretion, by which urea and other matters are passed into the blood, and bile also may enter the circulation when its excretion is impeded.

The skin, the sclerotics, the lining of the arterial system, the mucous membranes generally, all normal secretions and pathological exudates, and all parts of the body except the teeth, the hair and the glans penis may be tinged with the icteroid hue, varying from light yellow to darker shades with greenish admixture. In certain cases the feces are nearly colorless, clay or putty colored, but as their color is due to the presence of both the biliary and the pancreatic secretions bile may not be absent even from light-colored feces if the pancreatic juice is deficient. An important train of nervous symptoms results from jaundice, probably due to the presence of biliary acids and salts in the circulation rather than to the pigments.

## Peritoneum.

**Malformations.**—Imperfect development of parts of the peritoneum have been described, especially of the omentum; excessive length of the mesentery permits volvulus, and other folds, if too long, allow the organs to which they act as ligaments to fall to lower levels (enteroptosis). Fissures in the serous folds may allow portions of the gut to pass through (hernia), and similar results occur in pouches on the abdominal walls.

**Disorders of Circulation.**—*Active hyperemia* is observed in the first stage of peritonitis, general or in scattered areas, and about tubercles and tumors there may be a zone of congestion. *Passive hyperemia* follows from obstacles to the portal circulation and in long-standing cases the vessels may become much dilated, especially the veins along the line of reflection from abdominal organs to walls, as in cirrhosis and tumors of the liver.

Slight *hemorrhage* into the peritoneum or beneath it may occur in portal obstruction, phosphorus-poisoning, death by asphyxia and some other conditions. Large collections of blood in the cavity result from rupture of organs (spleen and liver), of aneurysms, injuries and operations on various organs, tubal pregnancy, typhoid and other intestinal perforations. The blood collects in dependent parts of the cavity and may be fluid or coagulated; even large quantities may be absorbed and the corresponding lymph nodes are deeply colored with it.

*Serous accumulations* in the abdominal cavity (ascites, dropsy) occur without local inflammation in general hydremias, as in chronic nephritis, valvular heart disease and cachexia. In other cases the peritoneum alone contains fluid, as when there is marked and prolonged portal stasis, commonly observed in atrophic cirrhosis. With inflammation and local diseases such collections are found in tuberculosis of the peritoneum and

tumors, with diseases of the thoracic duct the fluid is chylous. The ascitic fluid is usually clear, bile-stained in some cases, mixed with flocculi of fibrin, varying in amount from a few cc. to many liters, distending the cavity, pushing the diaphragm and organs upward and causing dyspnea, producing white scars in the corium from rupture of its fibers. When removed by tapping the ascitic fluid may renew itself many times. Adhesions, may localize it and cause sacculated dropsy, and if between the layers of the omentum it is called omental dropsy.

*Injuries* of the peritoneum are dangerous from exposure of the membrane to the air, contact with rough foreign substances, and access of bacteria; under aseptic conditions and supplied warmth and moisture surgical wounds are almost without danger to the healthy peritoneum. Injuries which involve the alimentary canal also, with exit of its contents, are especially liable to end in severe inflammation.

**Inflammation.**—The peritoneum has a superficial extent about equal to that of the entire surface of the body, it is in constant movement, both in the layer lining the anterior wall and in the visceral layer, its power to absorb various fluids is enormous, its vascular and nerve supplies are abundant and it is in close relation to important organs, vessels and nerve centers; hence a general inflammation of the membrane is necessarily of great clinical importance.

While primary idiopathic peritonitis may occur, in the vast majority of cases the inflammation follows access of pyogenic bacteria, either through the blood-vessels, which is infrequent, or by extension from organs already inflamed, or by perforation of certain parts, especially of the intestine. The first may occur in pyemia. The second arises in many ways but the only normal opening from the peritoneum to the outside world, the Fallopian tube, is worth specially mentioning in this relation because of the frequency of peritonitis in the female, from gonorrheal and other salpingitis, puerperal infections and other genital conditions. The third variety follows strangulated

hernia, ulcer and perforation of the gut, abscess and tumors and injuries of any of the abdominal organs.

*Peritonitis* is described as localized when but a small part of the membrane is affected, or general when most of it is attacked; either may precede the other, for a local inflammation may become general and the latter may subside and leave a chronic circumscribed process. The area attacked becomes actively hyperemic, loses its luster, and soon is the seat of an inflammatory exudate. This may be serous or purulent from the first, but is often fibrinous, and the effect is to bind together adjacent surfaces and so limit the extent of the disease. Later the fibrin is liable to become purulent and if capsulated an abscess is thus formed in a pocket between certain coils of intestines. When this remains, the pus may thicken and become absorbed, fibrous tissue and lime salts completing the healing process. At times the pus burrows for long distances, and is voided through some hollow organ or externally. If the abscess rupture into the rest of the cavity a general and rapidly fatal peritonitis may result. This is also the usual case when the amount of irritating material is large or very septic, as with strangulated hernia, multiple bullet wounds of the gut, or rupture of the gall-bladder. In such cases the lesion may deserve the name of gangrenous peritonitis. A hemorrhagic variety is also described, which is merely an expression of such local or general conditions that extravasation and hemorrhage easily occur, as in scorbutus.

*Chronic peritonitis* may follow the acute form, especially when encapsuled, or it may be limited in extent and of slow type from the first. A form of this variety is at times seen in the upper zone of the abdomen, resulting in thickening of the capsule of liver and spleen. The thickened membrane has been thought to resemble sugar after melting and hardening, and has received the German name, suggesting this, of "Zuckergussleber," another instance of the unfortunate choice of pathological terms from the diet list. Chronic peritonitis is common

in the pelvis, especially of women, and results in organized bands of adhesions between the contents of the cavity and of the abdomen proper.

**Infectious Granulomata.**—The only important disease of this kind affecting the peritoneum is *tuberculosis,* which is very rare as a primary infection but common as a sequel of similar disease in the alimentary tract, its lymph nodes and other organs. It may occur as a general miliary tuberculosis of the entire membrane; it may be limited to small miliary masses on the serous coat corresponding to ulcers on the mucous coat of the intestine. Various groups may coalesce and form large masses of thickened tuberculous tissue, or it may produce increased thickness of the omentum and various adhesions between intestinal coils so that it is impossible to unravel the abdominal contents. Copious transudate of serous fluid accompanies some forms of peritoneal tuberculosis, which is always a chronic process, and the fluid, either sacculated or free, in some cases may be reabsorbed and the process ends in apparent recovery.

**Tumors.**—Chronic peritonitis is at times accompanied by the formation of many small fibromata (or endotheliomata) over the serous surface, giving the effect on first sight of tuberculosis. Lipomata develop in the omentum quite frequently, fibroma and fibrosarcoma of the broad ligaments are also found at times.

Primary carcinoma is rare, though it may take origin in fetal remnants, as of portions of the alimentary tissues constricted off during development. Colloid or gelatinous carcinoma occurs with similar disease of the caput coli, rectum, etc., and at times is diffusely spread over large areas in miliary or larger nodules. Similar conditions occur in general carcinomatosis. Other organs from which carcinoma may invade the peritoneum are the uterus and ovaries, stomach and liver, and even the pleural contents by extension through the diaphragm. In all forms

a certain amount of serous exudate may be found, at times hemorrhagic, and various adhesions between the viscera are common.

**Parasites.**—There seem to be no strictly peritoneal parasites, but distomum hepaticum and echinococcus from the liver, filaria from the blood and lymph channels, actinomyces from the cecum and the kidney, and a few others have been found.

# CHAPTER XVIII.

## THE URINARY SYSTEM.

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### Kidney.

**Malformation.**— In viable infants one kidney may be lacking, usually the left, and the right, often provided with two ureters, is then large enough to perform the entire renal function. The division into lobes, normal in the fetus, is usually lost about the tenth year, but may persist to adult life. Extra kidneys are uncommon. The two organs may be united at the lower ends by fibrous or renal tissue, forming a horseshoe kidney, the pelvis usually lying on the anterior aspect of the double organ, with anomalies in ureters and vessels. United kidneys, and either one singly, may lie below the normal level, at the pelvic brim, or even within the cavity.

As an acquired dislocation the right kidney falls forward and downward from looseness of its ligaments, less often the left, which is more liable to congenital displacement. The cause of such a floating kidney may be pressure of the mass of the liver, owing to right-sided pleural distention, or pressure from without, and at times traction from the stomach and transverse colon appears to have the same effect. The motion takes place along an arc of which the renal vessels form the radius, and is of considerable extent when the perirenal fat is deficient. As the condition tends to become more marked the radius lengthens, the range of motion increases, the nerves and vessels. the ureters and other structures, are dragged upon and severe symptoms develop. Among these are pyelitis and hydronephrosis, intense pain, and pressure effects.

**Disorders of Circulation.**—*Anemia* of the kidneys occurs with general anemia from any cause, and at times, even when the organ was probably hyperemic during life, it appears bloodless on autopsy. This may be due to the swelling of the epithelium in the edematous cortex, or from post-mortem coagulation, which mechanically drives the blood out. The glomeruli may appear as dark-red spots on a pale background, for their arterial tufts remain full. With true anemia the whole organ is pale and small.

*Hyperemia.*—The kidney is the one organ in which the difference between active and passive hyperemia is apparent after death, owing to the peculiarity of its circulation. Arterial hyperemia seldom occurs without added signs of degeneration or inflammation. It may be found as the result of irritating substances excreted through the kidney, as cantharides, carbolic and oxalic acids, and in scarlet fever and extensive superficial burns, when death occurs before inflammation develops. The kidneys are then equally affected, large, succulent, the capsule strips off readily (in the absence of previous disease), the cortex is swollen and edematous, dark red, and markings often very distinct, glomeruli distinguishable on gross inspection, the pyramids less congested.

*Passive congestion* commonly results from general circulatory disorders, valvular heart disease, emphysema, fatty degeneration of the myocardium and similar conditions, though obstruction of one renal vein will produce stasis in the corresponding kidney, and of the vena cava, in both. In an acute form renal stasis occurs with death from asphyxia. When simple, passive congestion results in a large kidney, capsule not adherent, juicy, surface smooth, venous stellulæ prominent, cortex swollen and dark red, glomeruli prominent (a hand magnifying glass may be needed), pyramids also dark or brownish-red. This condition of stasis, like that of active hyperemia, seldom lasts any time without resulting in degeneration of the epithelia or increase of fibrous tissue or both.

*Hemorrhage* in slight degree may follow severe congestion of either form, enough to appear in the urine as individual red cells, and may usually be considered as simple diapedesis. Injury of the organ, purpura and hemophilia, and tumors may be accompanied by larger bleedings when affecting the kidney. With infarcts hemorrhage is common.

*Thrombosis* of small renal veins may occasion but little disturbance; when the larger branches are affected the kidney becomes congested and edematous, and fatty degeneration or necrosis occurs in the part involved.

*Embolism* is more common and more important, for the renal arteries do not anastomose. The result of embolism is anemia of the part supplied, in the usual wedge- or cone-shaped form, with the base superficial. Red infarction is less common in the kidney than the anemic form. The usual steps toward healing, death and resorption of the cells, invasion peripherally by new vessels and connective tissue, scar formation and contraction, follow rapidly and the capsule may be adherent over an area of firm, yellowish, depressed fibrous tissue, the site of the infarct. Such conditions may be multiple and not limited to the surface of the kidney. Other forms, leading to suppuration, will be treated under a later heading.

*Atrophy.*—Loss of function, diminished blood supply and pressure upon the kidney lead to atrophy of its functionating epithelia; hence it both accompanies old age as a senile change, and is the usual result of damming back the flow of urine so that the organ is distended from within. In old age the atrophy may affect the cortex almost entirely, especially the subcapsular layer. The surface is then granular, or rather it presents a number of fine depressions, and the epithelium corresponding is degenerated, pigmented or lost, the glomeruli are small and their capsules thickened. If the whole organ is involved it is small, tough and pale or brownish. A replacement fibrosis may be added and the organ is distorted by the fibrous contraction. This form is closely associated with arteriosclerosis, usually

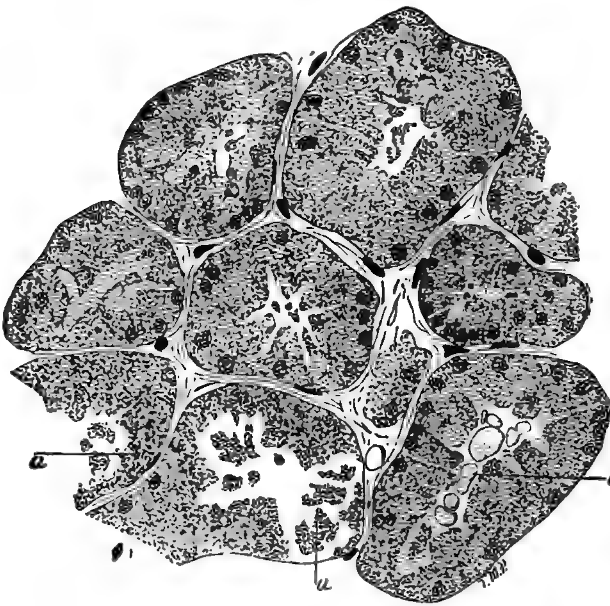
general throughout the body, at times manifested chiefly in the kidney. All parts of the organ may not be involved, but here and there the thickened vessels produce areas of atrophy and shrinking, often with lime salts deposited in them, and the urinary tubules, being compressed while excretion goes on above, dilate and form little retention cysts, both on the surface and through the tissue. The capsule may be adherent, the surface is always granular over these areas. Such arteriosclerotic atrophy of the kidney is common in gouty patients, after chronic lead-poisoning, and in the syphilitic. Similar effects follow endarteritis obliterans of the renal vessels, as so often associated with chronic inflammation. Hence a series of kidneys might easily be collected illustrating these various conditions and combinations of them and transitions between them, so that for purposes of description artificial boundaries have to be assumed which in practical experience are seldom noted.

*Hypertrophy* of one organ follows degeneration and disease of the other as a functional and compensatory change. It may be congenital, when one kidney is cystic or the seat of a tumor, it may be acquired late in life when a kidney is diseased, and is of great practical importance in surgical removal of the organ. The one hypertrophied presents both an increase in the size of its elements and also in their number and hence is a combined hypertrophy and hyperplasia. The general condition of the patient and the constitution of the urine may be perfectly normal with such compensatory hypertrophy.

**Degeneration.**—*Acute renal degeneration* is usually of the albuminous variety and as "cloudy swelling" accompanies many febrile diseases and the action of certain poisons and irritants. Among the former, typhoid and scarlet fevers, diphtheria and septicemia, pneumonia and others commonly result in cloudy swelling of various organs, especially the kidneys, and the explanation is probably that their toxins (as well as the bacteria) are excreted through the organs, and poison the

cells by chemical action on their protoplasm. This resembles the action of arsenic, mercury and phosphorus, cantharides and other substances more commonly known as poisons. In slight degrees the effect of such action is to cause the epithelial cells to swell and become opaque, from the presence of fine or

Fig. 106.




Acute Parenchymatous Degeneration of the Kidney. (*Delafield and Prudden.*)

*a*, epithelial cells, degenerated and desquamated, the nuclei preserved in places; *b*, hyaline material in the lumen oi the tubes.

coarser granules in them; congestion and slight edema commonly accompany this condition. More pronounced action leads to fatty degeneration and coagulation necrosis of the epithelia.

Acute nephritis may follow or accompany the effect of such toxic influence, as is well illustrated by the usual phenomena

in scarlet fever, where with a mild case and in the beginning degeneration occurs, later acute exudative nephritis, and still later, often after the fever has disappeared, acute productive nephritis. Apparently these three degrees correspond to the intensity of the toxic action, the cells reacting but not dying with slight degrees, degenerating with stronger doses, and the effect passing over to the stroma with the highest degree of influence. The gross appearance of the kidney in simple cloudy swelling is slight increase in size and succulence, the capsule strips readily, the cortex is swollen and pale and its cut surface is opaque as if dashed with hot water. It may also be moderately congested.

*Fatty Degeneration.*—Fatty infiltration occurs only where fat is normally present; as this is not the case in the human kidney a fatty degeneration is the only change of this character which can be described. It follows the albuminous form both in febrile cases and in poisoning, especially with phosphorus, and may occur also with no sign of inflammation, either exudative or productive, as in anemias of various kinds. It occurs in cachexia, as with chronic tuberculosis, and is a regular attendant upon inflammation both acute and chronic. The element common to all these is defective nutrition of the epithelia with or without added toxic action.

The fat may be limited chiefly to the region of the convoluted tubes, and if absorbed the result may be minute depressions over the cortex. When general, fatty degeneration produces a large pale kidney with a decided yellow look unless there is much congestion with it. The fat is usually visible to the naked eye as minute yellow points in the course of the urinary tubules; either in the cortex, where alternating blood-vessels and fatty tubes give a peculiar distinctness to the markings; or in the pyramids, where the long collecting tubes radiate like fine yellow lines on a darker background; or in both places. Such general fatty degeneration is not uncommon in the later months of pregnancy. When nephritis coexists the

gross and microscopic appearances correspond, as will be mentioned in discussing nephritis.

*Amyloid Degeneration.*—The causes of this variety are those of all amyloid change, suppuration in bones and in the lungs, as common in tuberculosis of these organs, syphilis, and other cachectic conditions, but the kidney seems especially liable, being affected when other organs escape. The organ may be large and yellowish, firm to the touch, friable, pale or mottled, and usually the gross appearance is a combination of fatty and amyloid degeneration. The capsule may be adherent, the surface usually is smooth, the cortex increased in size and marked by grayish lines, corresponding to the altered vessels, with yellow spots of fat. The application of iodine makes the amyloid portions prominent.

In other cases the change is limited to the smaller vessels or the glomeruli and can be detected only on microscopic examination. The slighter degrees are not accompanied by widespread fatty change because the vessels may still be open enough for the nutrition of the epithelia; these cells are not directly involved in the amyloid change but the membrana propria may show evidences of it. Clinically the results of amyloid degeneration are oliguria, albuminuria, general edema, and nervous symptoms with coma or convulsions.

Glycogen and fat together occur in the kidneys of diabetics, especially in the cells of Henle's loops, and in kidneys hardened in absolute alcohol the addition of iodine develops the characteristic brownish-red color.

Lime salts occur in the form of "infarction" of the urinary tubules, and in the new-born are taken to signify that the child has breathed (their absence does not prove the opposite). Similar deposits occur in glomeruli which have atrophied, in degenerated epithelia, and accompany various inflammatory and toxic conditions.

**Inflammation.**—The importance of the renal function, the certainty that toxic substances in the blood will sooner or later

reach the kidney, the rapidity with which irritation leads to degeneration and inflammation, the liability of the organ to both active and passive hyperemia, and the great resemblance clinically between various diseases of the part, have together produced a confusion in the pathology of the kidney which makes the subject particularly difficult to present or understand. The name nephritis, with qualifying adjectives, has been given to congestions, degenerations and inflammations, so that it resembles the expression "Bright's disease" in conveying more than one idea. It is still possible to arrange the lesions of the kidney in an orderly manner and to remember that they tend to combine and to pass from one into the other, and that all non-inflammatory lesions may become inflammatory, and that any acute form of nephritis may become chronic if the patient lives long enough.

*Etiology.*—Injury, severe chilling of the surface, burns and scalds, ingestion of poisonous and irritating substances, and many bacterial toxins may cause inflammation of the kidney, which, as distinguished from the more common clinical types, might be called primary.

As a general rule, however, nephritis is associated with some other lesion. This may act by circulatory disturbances, as in lung and heart disease; or by the excretion of toxic substances formed in the body, as seen in connection with long-standing intestinal dyspepsia and absorption from the decomposing contents of the gut; or perhaps general conditions of malnutrition, as in tuberculous, syphilitic, cancerous, anemic and other cachexias. In many other cases we may assume the action of a toxin derived from one or more bacteria, with presence of the microörganisms in the kidney itself (embolism by pyogenic cocci, anthrax, etc.), or excretion of toxins alone. Among the poisons arsenic, phosphorus, carbolic and oxalic acids, mercury, lead, cantharides and turpentine may be mentioned. Among the diseases with the presence of microörganisms in the kidney may be mentioned pyemia, mycotic endo-

carditis, malaria, anthrax, pneumonia, typhoid fever, and various suppurative diseases due to pyogenic organisms, cocci, b. coli communis, b. pyocyaneus, gonococci, and others. As an example of toxin alone (probable in many cases), cholera, diphtheria, variola and inflammatory rheumatism may be mentioned.

The locality most often involved is that of the convoluted tubules and the glomeruli; indeed the latter may be so nearly the only part affected as to justify the term "glomerular" nephritis, as in poisoning by cantharides and chlorate of potash. In other cases, especially the chronic forms, no element of the organ escapes. Again, as a rough rule, it may be stated that in the acute forms of nephritis, without suppuration, it is the epithelium which especially suffers, while in subacute and chronic inflammations the fibrous stroma presents the chief lesions and the epithelia suffer in consequence of these.

The various forms of nephritis are:

- Nephritis
  - acute
    - exudative
      - catarrhal.
      - hemorrhagic.
      - suppurative.
    - productive—diffuse.
  - chronic
    - exudative—large white kidney, chronic diffuse nephritis.
    - productive—cirrhotic kidney, chronic interstitial nephritis.

*Acute Parenchymatous Nephritis.*—Acute Bright's, glomerular, catarrhal, or tubal nephritis.

In acute exudative nephritis the exudation may consist, as elsewhere, of serum, fibrin and pus, with diapedesis of red cells, and the resulting type of the disease depends in great part on which of these is most abundant. If serum predominates, though both red and white cells may be present and fibrin also, the form often called catarrhal or desquamative results. Congestion regularly precedes and accompanies all varieties. The

glomeruli may be chiefly affected or the tubes or both, and during life the urine contains serum, casts and relatively few leucocytes and red cells. This form may follow exposure to cold, and often accompanies pregnancy and infectious disease, especially scarlet fever. The epithelia may be the seat of cloudy swelling or of more serious degeneration, but the essential pathological element is the condition of the blood-vessels which permits exudation, of serum especially.

The organ is swollen, capsule not adherent, surface smooth and congested or pale or mottled, succulent, cortex swollen and cloudy, glomeruli at times very prominent. Microscopically the discoverable lesions may be out of all proportion to the clinical gravity of the case; there may be only a few casts in the tubules with evidence of congestion, and in the glomeruli distended arterial tufts and desquamation of the lining cells. Severe cases show more marked lesions, the epithelia in the cortex may be swollen, compressed, detached from the wall, or degenerated; the tubes are distended with (probably) altered fibrin and may contain red cells beside epithelia and leucocytes; in the urine these appear as hyaline casts and separate cells, with albumin. In the glomeruli the capillaries may be congested or not, but the covering and lining epithelia are swollen, desquamated and degenerated more than in the milder cases, even to complete filling of the capsule of Bowman. In the cortex here and there small collections of white cells may be found, which differ from abscess formation in the preservation of the cells and the absence of bacteria.

*Acute Hemorrhagic Nephritis.*—While the former variety may be fatal in a comparatively few hours, it is possible to recover from it without serious damage to the kidney tissue, and this is the rule in mild cases. When the intensity of the producing cause is such as to result in great numbers of red cells escaping from the vessels, as in malignant endocarditis and scarlatina, some cases of carbolic and other irritating poisons, the gravest form of infectious or toxic acute nephritis

occurs. The kidney is usually very large, soft, congested or pale, but marked everywhere in the cortex by smaller or larger points of extravasation, of a deep red color, corresponding to the hemorrhages. With infection these areas may be entering upon suppuration. While this is but one variety of exudative nephritis it differs from the foregoing in being uniformly fatal.

*Acute Suppurative Nephritis.*—This condition, which is marked by exudation of pus-cells and the formation of abscesses, may be due to extension of inflammation from the pelvis of the kidney (ascending suppurative nephritis) and this form will be treated under pyelitis.

It may also be connected with pyogenic organisms in the circulation, as in mycotic endocarditis, infectious osteomyelitis, pyemia and other distant diseases with suppuration. In a chronic form it is often associated with tuberculosis of the kidney. The microörganisms are the pyogenic cocci, b. coli communis, and as perhaps a causal, perhaps an accidental find, typhoid and pneumonia organisms. The first step in the process is embolism of the renal capillaries by the bacteria, with necrosis of the cells and a zone of reactive inflammation. These areas rapidly become small abscesses and the organ may be dotted with them, or they may coalesce and form large cavities. The pus finds its way out by the ureter or burrows into the perirenal tissue or remains in situ. Usually both kidneys are affected but even then one may show far more damage than the other.

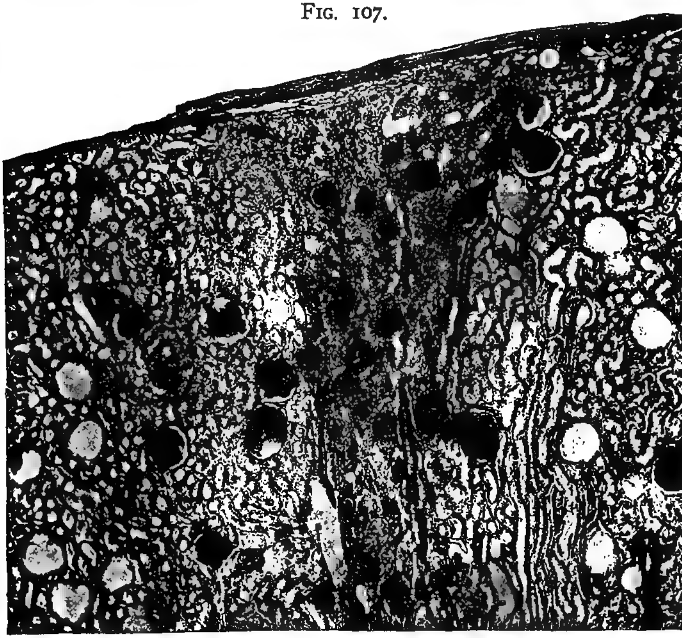
As a result of injury, part or the whole of a kidney may be crushed, with the production of one or more small purulent foci or conversion of the whole organ into a mass of pus and broken-down tissue.

*Acute Productive Nephritis.*—Subacute diffuse nephritis, "wedge" kidney.

This form of acute nephritis might be called exudative-productive, for its histology is a combination of both characters. Even when death occurs early in the disease the pro-

ductive change has already begun. In many cases the distribution of the new fibrous tissue is along the arteries running to the cortex. This results in the formation of long slender cones about the vessels, their bases on the surface, which is depressed by their contraction. These are usually

FIG. 107.



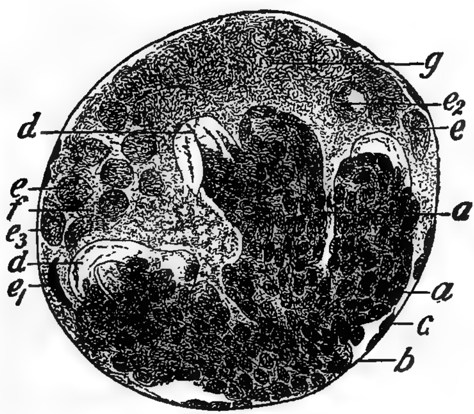
ACUTE PRODUCTIVE NEPHRITIS. (*Delafield and Prudden.*)

**In the middle a conical "wedge" of fibrous tissue about an interlobular vessel. Epithelia in this area lost. Glomeruli here are atrophic, elsewhere many have fallen out of the section.**

termed "wedges," but this view takes in only two dimensions while the development of new tissue occurs in three, the mistake arising from the fact that the organ must be cut open before the change is noted and then a flat surface presents.

Such fibrous increase may occur also scattered through the tissue. In the older cases this new tissue is very poor in cells. The other microscopic changes are swelling or degeneration and atrophy of the epithelia, formation of casts, desquamation of the glomerular lining with at times marked hyperplasia of these cells and pressure upon the arterial tufts. Moderate exudation is present early; later there may be but slight trace of it. Lymphocytic infiltration may be profuse.

FIG. 108.




PROLIFERATION AND DEGENERATION OF GLOMERULAR EPITHELIUM. (*Ziegler.*)

*a*, normal capillary loop; *b*, capsule of Bowman; *c*, epithelia of capsule; *d*, vascular loops denuded of epithelia; $e_1$, $e_3$, desquamated degenerated glomerular epithelia; *f*, *g*, exudate between the cells.

The gross appearances of such kidneys are increase in size, non-adherent capsules, smooth red or mottled surface, cortex marked by the "wedges" described above, with dimpling of the surface over them; these occur also in chronic nephritis.

The results of acute productive nephritis are always worse than those of the exudative form if the patient survives the first attack, for the kidney is permanently injured by a fibrosis

which like the same process in other organs has a tendency toward persistent increase. Attacks of this kind are common after diphtheria, scarlet fever and with pregnancy.

## Chronic Nephritis.

The essential element in either form of this lesion is the marked fibrous increase in the stroma of the organ with consequent changes in the epithelia, but in some cases there is an inflammatory exudate (serous) which appears in the urine in relatively large quantity and persistently, and with this the case is remarkable clinically for general dropsy. While the lesion then is productive, the exudation distinguishes the disease from the pure chronic productive nephrities in which there is no albuminuria, or only an occasional appearance of this symptom, and anasarca is commonly absent.

In *chronic exudative nephritis,* as in the other form, all the elements of the organ are involved. The cause may be a preceding acute nephritis, or chronic passive congestion of the organ, and this factor enters in with any cases which complicate pulmonary tuberculosis, emphysema, valvular cardiac disease. Other cases follow syphilis, lead-poisoning, gout, alcoholism, and in the latter there is often hepatic cirrhosis as well. In the young, nephritis of this type may develop after scarlet fever or without apparent cause.

The gross appearance of the exudative form of chronic nephritis varies, but commonly the organs are enlarged. In color they may be white from combined anemia and fatty degeneration but they may be mottled or dark red in proportion to the congestion present. The capsule in many instances is not adherent and the surface is smooth, in kidneys of smaller size the capsule may be so adherent that little grains of kidney tissue are torn off with it and appear on its inner aspect in scattered groups. Larger masses of tissue may be torn off

where a vein passes between capsule and organ, but this will hardly be confused with the dotted groups mentioned.

In the smaller forms of kidney, when the fibrous tissue has contracted a great deal, the surface of the organ is often marked by small cysts with clear pale contents or thicker and dark yellow or green fluid, or the former site of such cysts may be marked by little puckered scars. These retention cysts are more common in the next variety. The cortex may present but little change beyond swelling and paleness, or it may be congested and at times dotted with punctate hemorrhages. In other cases the fibrous cones are well developed and scar-like bands of tissue run from depressions on the surface into the organ. The markings of the cortex are commonly not well preserved.

Microscopically the appearances differ with the age of the process. In recent cases, where death has occurred fairly early, there is well-marked and general degeneration of the epithelia with scattered foci of new fibrous tissue, rich in cells, which may communicate by fibrous processes. Spindle cells and delicate fibrils may be found. The process is specially developed about the blood-vessels and the glomeruli. In the latter the capsule is thickened, the lining cells are increased in number and degenerated, but many glomeruli appear nearly normal. While the main effects of the process are most apparent in the cortex the increase in the stroma and the epithelial degeneration may be found in the pyramids also. The urinary tubules may be atrophic, filled with degenerating epithelia and coagulated fibrin, or dilated; both red and white blood-cells may occur in their contents. In the glomeruli some of the capillaries may be the seat of amyloid changes as also other vessels; a certain degree of arteritis is common, with thickening of one or more coats and diminution of the lumen.

*Chronic Productive Nephritis.*—Chronic Bright's, interstitial nephritis, cirrhosis of the kidney.

In this form the rule is that the kidneys are very atrophic; they may weigh together much less than the single normal organ; rarely they are larger than normal. The capsule is adherent, often stripped off with difficulty, and the fatty capsule may be increased to make up for the loss of volume in the atrophic organ. The surface is very granular, frequently presents cysts, which are found also in the interior, the cortex is

FIG. 109.

CHRONIC INTERSTITIAL NEPHRITIS. (*Delafield and Prudden.*)

Marked fibrous hyperplasia about the glomerulus, which is also thickened. Epithelium degenerated, cell bodies granular, nuclei absent in places.

irregularly thinned and its markings lost on gross examination. The new fibrous tissue is irregularly disposed through both cortex and pyramids; the pelvis may be widely dilated to compensate for atrophy, or when the nephritis follows obstructed flow of urine. Chronic catarrhal inflammation is a frequent complicating lesion

Microscopically the glomeruli, vessels and tubes present the same atrophic and degenerative conditions as in the former variety. In other words, so far as the histology of chronic nephritis is concerned all forms might be described together; the distinction made here is justified by the differences in the clinical course of the two, and each may be recognized by the symptoms.

With the latter form hypertrophy of the left ventricle is usually more marked than with the former, not due so much to the changes in the kidney as to the general arterio-fibrosis throughout the entire system of arterioles. This multiplies the work of the left side of the heart both by increasing the friction against which it has to labor, and also by depriving it of the vascular recoil or peristaltic wave, which takes up the charge received after each systole and carries it to the capillaries without additional tax upon the heart. The retention of water in the body because of lessened urinary excretion, and the retention of various chemicals which act as irritants to the heart, have also been held to explain the cardiac hypertrophy and the pulse of high tension in these cases. When one remembers that the adult kidney should excrete in twenty-four hours from 28--40 gm. of urea, 10--15 gm. of chlorides, 2--6 gm. of phosphates, 1 gm. uric acid or urates, and 20 mg. of oxalic acid; and recalls the effect of perfusion with various solutions upon the hearts of animals; it is evident that hypertrophy of all the cardiac chambers in chronic nephritis may be due to retained excreta. The result in the heart is so large an increase in its tissue as to warrant the name *cor bovinum*. It is in this form that hemorrhage into the retina or the brain is especially common, as might be expected from the combination of degenerated arteries and powerful systole. (p. 345.)

Uremia and its explanation have been mentioned in Part I., p. 57.

**Cysts of the Kidney.**—Dermoid cysts rarely occur. Small retention cysts are common in senile atrophy and in chronic

interstitial inflammation. Occasionally a kidney, normal in other respects, presents a single fairly large cyst in the cortex; probably due to closure of tubules by mineral matter (calcium salts) with local inflammation and stenosis of the tube. In some cases an entire kidney is converted into a multilocular cyst as the result of calculi in the opening of the ureter and consequent dilatation by accumulating urine behind the obstacle; the kidney tissue may be recognized here and there as a thin peripheral film.

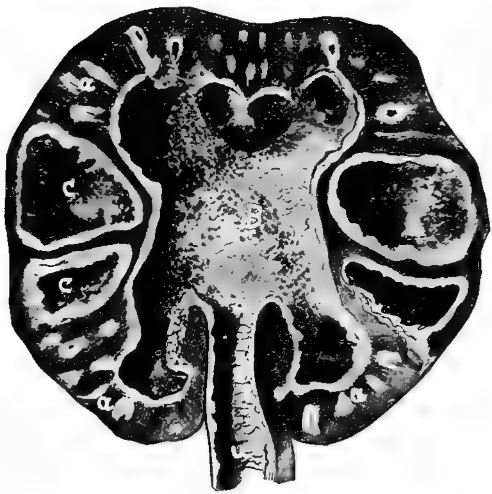
A similar condition occurs, usually in one kidney, associated with atresia of the papillæ, as a congenital anomaly.

**Tumors.**—Fibroma, lipoma and leio-myoma sometimes occur in the kidney; the first may attain a large size, the others are usually small. Sarcoma of the organ is rare but myo-sarcoma, with striate cells, has been described.

*Hypernephroma* is usually benign if small, and malignant when larger; it starts in adrenal tissue included in the kidney during fetal life. The tumor corresponds in its structure to that of the adrenal body but the relative proportion of cortex is apt to be larger and its blood supply is usually rich (capillaries). Bleeding and cavernous forms are not uncommon, recognizing that hypernephroma is in itself a rare tumor, and as in other neoplasms of the organ, glycogen is frequently present. The cells may be arranged as solid columns with no glandular lumina, or as double rows, each ending in rounded crypts and enclosing a lumen. The malignant forms cause metastasis to various organs owing to the ease of transmission through the dilated capillaries, and with malignancy the normal adrenal structure gives place to irregular atypical cells and newly formed vessels with degenerated (hyaline) walls. *Adenoma* may start in hyperplastic areas of renal cells, as in similar hepatic conditions, and this form of tumor may become cystic. *Adenosarcoma* occurs in early life and often becomes malignant after a period of latency. Primary *carcinoma* is not common in the kidney; it occurs in late adult life and in

most cases begins in the epithelium of the cortical tubes. Metastases are not so common as in carcinoma of other organs. Secondary tumors of this variety frequently occur in the kidney, usually betraying their embolic origin as minute scattered nodules in the cortex.

FIG. 110.



LATE LESION IN TUBERCULAR PYELO-NEPHRITIS. (*Ribbert.*)
*b*, pelvis; *c*, calices; *u*, ureter; all dilated and covered with caseous pyogenic membrane; *a*, foci in collecting tubes.

**Infectious Granulomata.**—Primary *tuberculosis* of the kidney is very rare. As a secondary lesion it occurs in general miliary disease and with tuberculosis of the urinary and genital organs of the pelvis. The spread of the disease is usually upward, against gravity, though when the patient is lying down gravity is negligible; rarely it begins in the kidney or its pelvis and spreads down; and the entire urinary system, kidney, ureter and bladder, is commonly affected together. The disease is more common in males.

The kidney presents one or more, usually several, tubercular abscesses, with caseous contents, or empty and clothed with a pyogenic membrane. Corresponding to the upward course of the disease, the pyramids may be nearly all replaced by such abscess cavities while the cortex shows but little change, or the surface of the organ may contain miliary tubercles and scar tissue. Later on the entire interior of the thickened capsule may be filled with thick pus and caseous material. The lesion may be the only tubercular process, or pulmonary disease may also exist. What kidney tissue remains may be congested or in a condition of chronic inflammation or atrophy. If one kidney is involved the other may be the seat of chronic nephritis by the time the case comes to examination, but as the course of the disease is very slow, probably the other organ may be fairly healthy for long periods.

*Syphilis.*— Congenital syphilis may be associated with obliterating inflammation of the renal vessels and atrophy of the glomeruli, and similar effects with amyloid changes may accompany the acquired disease. Gumma in the kidney is rare but at times thick, stellate scars in the cortex appear to have had that origin.

**Parasites.**—Beside the bacteria which may be excreted through the kidney or lodged in it, aspergillus, oïdium albicans and actinomyces among the vegetable parasites, and echinococcus, cysticercus and pentastomum among the animal, have been noticed. In tropical countries the filaria sanguinis occurs in all parts of the organ, chiefly in its dilated lymph channels, and causes the condition known as chyluria. In these cases there may be chronic nephritis and a peculiar opaque and greasy look in the pyramids, with dilated and varicose lymph channels.

**Calculi, Pigmentation, Etc.**—In the new-born, from the second to the fourteenth day, collections of uric acid and urates occur in the large tubes of the pyramids; a similar condition is

not uncommon in the adult kidney with gout, and lime salts are found here in diseases of the bones. Biliary and malarial pigment may be found in the renal capillaries; disorganized hemoglobin remains after hemorrhages; ingested stains, like silver, more commonly affect the cells than the stroma of the kidney.

Calculi form in the pelvis of the kidney as fine sand, which passes out almost without symptoms, or larger sizes which cause severe attacks of renal colic, and yet larger stones with many projections which produce distention of the kidney, atrophy of its tissue, and reach up into the various dilatations of the calices. They are of the same chemical composition as the vesical calculi; see p. 543. Their effects on the kidney are partly due to irritation in the pelvis, which at times appears to be connected with the development of carcinoma, and partly due to the destruction of the kidney from damming back the flow of urine.

**Perinephritis.**—In the fatty tissue about the kidney contusions and other injuries may produce a suppurative inflammation, but more commonly this attacks the part by extension from caries of the vertebræ or inflamed retro-peritoneal lymph nodes. A distinction is made between perinephritis, inflammation of the capsule, and paranephritis, inflammation of the fat tissue about it, but one could hardly exist without the other and they do not need separate description. The collection of pus may be relatively large and compress the kidney, causing atrophy, or setting up suppuration in it; or it may burrow along the posterior abdominal wall and reach the pelvis, pointing under Poupart's ligament, in the vagina or finding a vent elsewhere. A chronic fibrous hyperplasia may convert the perirenal tissue into a dense mass of scar formation, and either this or the purulent form may arise in connection with chronic suppurative lesions of the kidney.

## Ureter.

**Malformations** of the ureter may be found as entire absence of one, common with horseshoe kidney, or one or both may be double for a part of its length or the whole of it; partial doubling commonly affects the upper end. The lower ends may blend and open by one orifice in the bladder or unusual terminations may occur, as in the vagina or the urethra.

With congenital or acquired stenosis of a ureter and preservation of the upper lumen, the part above the narrowing may dilate. The obstacle may be as far away as the prostate, which prevents complete emptying of the bladder when hypertrophied and thus causes urine to accumulate in the ureter and dilate its whole extent; or inflammatory adhesions or calculi may close the upper end and only the pelvis of the kidney dilates. When there is no inflammation in the pelvis the condition is called *hydronephrosis* and the retention of urine may be so great as gradually to destroy the kidney by pressure atrophy. Similar results may be caused in floating kidney, the organ falling enough to produce a sharp bend in the ureter which prevents the passage of urine. Outside pressure, as from tumors, is less often the cause.

*Hyperemia* in the ureter may follow the passage of mechanical or chemical irritants, calculi, poisons and parasites; the urine may contain blood from this cause.

**Inflammation** of the ureter, especially important in the pelvis of the kidney, arises from similar causes, extension of inflammation upward, alkaline decomposition of the urine and especially irritation by calculi. The inflammation in mild cases is a simple catarrhal process and may leave no effects; with pyogenic organisms the mucous membrane is more swollen and hyperemic and small submucous hemorrhages may occur. The exudate is purulent and mixed with desquamated epithelial cells, and in some cases ulceration and necrosis of the mucous

surface may follow (diphtheritic pyelitis). Such a purulent pyelitis almost invariably attacks the kidney tissue, causing acute intestinal (suppurative) nephritis.

*Chronic pyelitis* causes a thickened mucous membrane with shallow ulcerations, in which there may be a deposit of mineral salts derived from the stagnant urine, and often the contents of the dilated pelvis is composed of a mixture of pus, shreds of mucous membrane, urinary concretions and decomposed urine. The kidney may be the seat of chronic nephritis or suppuration, or of atrophy from the pressure, and these conditions are at times combined.

*Tuberculosis* of the renal pelvis, pyelitis tuberculosa, usually complicates similar lesions in the testicles, seminal vesicles or bladder. One or both sides may be involved. The disease is chronic in its course, and beside the lesions mentioned above, presents tubercular infiltration and softening of the walls. The process usually extends to the kidney also.

**Tumors.**—Small cysts and polypoid growths are not uncommon in the ureter; other tumors are almost always secondary to those of the kidney.

*Parasites* may pass through the ureter from the kidney or remain there for a time; as the distomum hematobium in chyluria, round worms from fistulous communication with the intestine and echinococcus from rupture into the tube.

## Bladder.

**Malformations.**—The most important is the result of imperfect closure of the parts in the anterior median line over the bladder, by which it lies exposed. It occurs most often in males. The organ may be apparently normal but usually its anterior wall is lacking and the congested prolapsed posterior wall lies in the hypogastrium; fissure of the urethra commonly coexists (epispadias). In the most severe form the intestine opens on the posterior wall of the bladder. Other uncommon

conditions are partial or complete division of the organ by an antero-posterior septum and absence of the viscus, the ureters opening into the urethra directly.

As an acquired condition the bladder may be much dilated by chronic obstacles to urination, with accumulation of the fluid, when the wall of the organ is apt to show marked hypertrophy of its muscular fibers with sacculated protrusions between them. Acute distention results in thinning of the wall and rupture is possible, either with or without injury such as falls and contusions.

In dislocations of the uterus, destruction of the perineal body and great dilatation of the urethra in women, the bladder may be inverted through the vagina, making *cystocele,* or prolapse through the meatus.

*Hyperemia* follows irritation by substances in the urine, calculi in the bladder, and accompanies inflammation of the organ itself and of other parts (puerperal metritis). It may lead to acute catarrhal inflammation. *Passive congestion* is the result of obstructed venous return, general or local, and causes varicose dilatation of the vesical veins and chronic cystitis. A severe form of hyperemia results from too rapid emptying of a bladder which for long periods has held large amounts of residual urine, as in the prostatic hypertrophies of old men; it may lead to hemorrhage and fatal syncope.

Other causes of hemorrhage are wounds, general diseases like purpura, ulceration, and tumors, especially if malignant.

**Wounds** of the bladder may result from cutting or piercing instruments, rupture when distended by jumping from a high place and alighting solidly on the heels or buttocks, contusions with fracture of the pelvic bones, pressure of the head in parturition with necrosis of the injured part. Fistulæ may be the result of ulceration in the bladder, softening of tumors, and abscess formation in the adjacent tissues. Fistulæ may connect two mucous surfaces, as bladder and vagina (bi-

mucous), or open externally, or burrow into the perineum or the thigh.

**Inflammation.**—*Acute Catarrhal Cystitis.*—Mechanical irritation by stones and foreign bodies, chemical irritation by decomposing urine or substances excreted in it (cantharides), extension upward from the urethra in acute and chronic inflammation or through the bladder wall in prostatitis, and organisms introduced in careless use of instruments, are the commonest causes of simple catarrhal inflammation of the bladder.

During life the mucous membrane is actively hyperemic; after death this may have disappeared. The bladder may be found nearly empty, corresponding to the irritability of the viscus during life, but if it contains urine therc is usually a copious sediment of deusquamated epithelium, mucus, pus-cells and crystals. The lesions may end in complete recovery or persist in a subacute or chronic form.

In *chronic cystitis* the mucous membrane, as in other places, becomes much thickened, polypoid growths form, there is constant and profuse production of mucus and desquamated cells, hemorrhages may occur and where they remain beneath the mucous surface the result may be deep pigmentation. Following these changes shallow ulcers often develop, in the lower segment of the bladder usually, and deposits of lime and other salts in the necrotic tissue occur. The muscular fibers hypertrophy most markedly when there is some obstruction to the flow of urine, such as prostatic increase or urethral stricture. The course of the disease may begin with such an obstruction, muscular hypertrophy follows which after a time loses its compensatory power, the urine accumulates and sooner or later undergoes fermentation from the entrance of organisms. Cystitis follows at once and converts the case from a simple to a very dangerous disease. Injuries to the spinal cord cause not only paralysis of the muscular fibers of the bladder, with accumulation of urine, but the nutrition of its walls suffers so

severely that the irritant urine causes rapid necrosis of the mucous membrane; to this condition the name diphtheritic cystitis has been given. Perforation into the peritoneum or the tissues of the pelvis may follow, with rapidly fatal peritonitis or gangrene of the soft parts.

*Phlegmonous cystitis* arises from extension of superficial ulcers of the mucous surface deeper into the wall, with suppurative inflammation; this may perforate into the pelvic tissues and cause phlegmonous paracystitis and involve the other pelvic organs.

The organism most commonly found in cystitis, beside the micrococcus ureæ which produces fermentation of the urine, is the b. coli communis which has so marked a pyogenic influence out of its proper habitat; less often the gonococcus, b. proteus and streptococci are the forms encountered.

*Tuberculosis.*—Occasionally tubercles develop in the bladder with pulmonary and intestinal disease, but most often the lesion is associated with invasion of the testicle (epididymis), seminal vesicle or prostate. Some cases appear to result from extension downward of renal tuberculosis but in the majority of cases the disease progresses in the other direction. The tubercles are usually found in the trigone, and spreading from here a large part of the lower half of the bladder may present the miliary forms or caseous and ulcerating lesions. Cystitis of chronic type always accompanies the disease and the mucous membrane may show ulcers which are not tubercular, sometimes partly covered with false membrane, as well as those which are clearly caseous. Deposit of urinary salts is common in such ulcers. The urine may be either alkaline or acid in reaction, and blood, albumin, pus-cells and tubercle bacilli are commonly found in it. The disease is almost unknown except in males, corresponding to the greater frequency of tuberculosis of the other genito-urinary organs in this sex.

**Foreign Bodies** are more common in the bladders of hysterical women than in the male bladder, and the list of such

materials introduced includes nearly everything which may be passed into the urethra.

*Calculi.*—The bladder may contain from one to hundreds of calculi, the more numerous being usually small, the single ones reaching a size of several cm. in diameter and a weight of 1,000 gm. While either sex at any age may suffer from the disease, it is most common in men in middle life or after. The stones may lie free in the bladder, and with several present opposed surfaces are often slowly ground into polished facets, or they may lie in diverticula between the separated fibers of the wall.

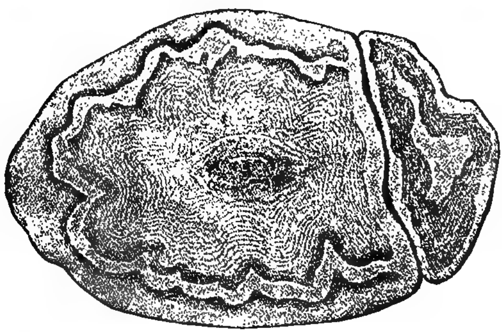
The form of the single stone is most commonly ovoid, seldom spherical; the surface may be fairly smooth or covered by small projections (mulberry form); the consistence varies from the hard urate calculus to softer masses of cystine, which if pure are wax-like; the color is blackish, gray or pale yellow; on section it is the rule to find concentric lines showing successive deposits, and a nucleus about which the process has started. Calculi of only one constituent are unusual, most often several varieties of mineral matter are found. Often a stone of one kind (uric acid and urates) will be the nucleus for the deposit of lime and other salts; this is called secondary calculus formation.

The process consists of alternate coagulation of organic matter about a nucleus and deposit in this of urinary mineral matters. The organic matter acts as a stroma to hold the inorganic elements together, and the latter may be dissolved out and leave the organic framework or the albuminous matter may be removed by digestion and leave the minerals. The nucleus may be a foreign body, as a bit of a catheter, a blood clot or a lump of inspissated mucus or albuminous matter, and a minute stone thus started may in turn become the nucleus for a different formation; but the various layers are always cemented together by coagulated albuminous matter and it is not uncommon to find a large stone covered by such material in which little spots of new deposit are forming. The stone may begin

to form in the renal pelvis (uric acid) and continue to grow after it reaches the bladder.

The results of vesical calculi are partly mechanical, injury to the wall by jolting, occlusion of the meatus internus so that urination is possible only when the patient is prone, and partly the result of inflammation, for cystitis is the rule with calculus. Straining at urination with hypertrophy of the detrusor fibers, pain, tenesmus, bloody urine, sudden stoppage of the stream, decomposition of urine and ammoniacal poisoning, residual

FIG. 111.



SECTION OF TWO VESICAL CALCULI. (*Ziegler.*)

urine and retention are the common results of the condition; to these must be added the pain and injury due to passage of small fragments through the urethra. Rarely the bladder wall is perforated by ulceration and the stone lodges in the pelvic tissues or passes into the vagina or rectum.

*Varieties* of vesical calculus (according to the material most largely present):

1. Uric acid; small, roundish, hard, smooth or granular, yellow, red or brown, concentric layers.

2. Urates; salts of ammonia and magnesia, often surrounded by phosphates, small, roundish or flattened, grayish or pale yellow, smooth or granular.

3. Phosphate of calcium; small or medium sized, rough, sandy surface, white with a gray or yellow tinge, hard, concentrically marked.

4. Triple phosphates; large, rough surface, grayish.

5. Calcium carbonate; small, white, friable.

6. Calcium oxalate; may be large, hard, brown, heavy, surface nodular.

7. Cystin; medium size, yellow brown, soft, round or ovoid.

8. Xanthin; small, ovoid, reddish-brown; these last two forms are among the unusual varieties; they may be the nuclei for phosphatic and uratic calculi.

**Tumors.**—Polypoid growths have been mentioned in connection with chronic inflammation; they are usually small. Fibroma occurs as a papillary tumor in the lower portions of the bladder and is very vascular, hence hemorrhages are common and may produce fatal anemia, bits of the tumor may separate and block the internal meatus, and chronic cystitis is commonly associated with the lesion. This tumor is a good example of a benign form with malignant consequences because of the accident of location. Carcinoma may develop upon such a basis, or be secondary to carcinoma of the rectum, cervix and vagina, prostate, testicle and other organs.

Parasites in the bladder occur as accidental results of fistulæ between it and the gut, or wandering oxyuris from the rectum, or rupture of echinococcus cysts into the ureters; filaria are abundant in chyluria.

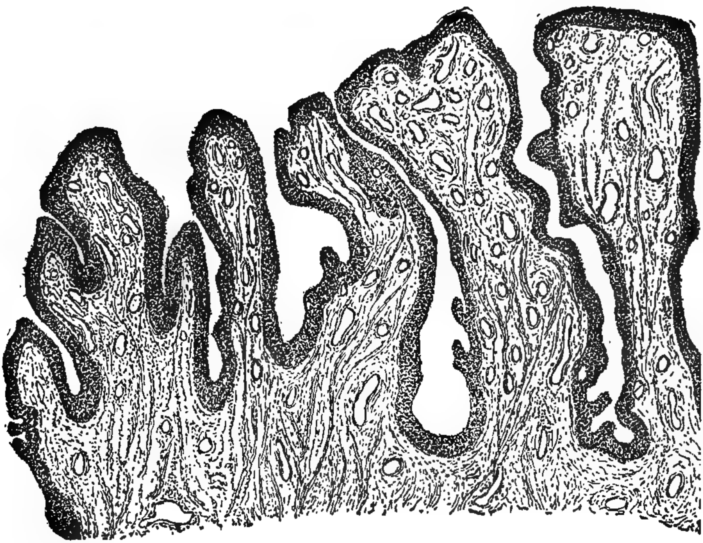
## Urethra.

**Malformations** are commonly imperfect closure of the tube, epispadias and hypospadias, non-development of a part, causing atresia urethræ, and variations in the passage of the tube through the prostate gland.

**Injuries** may be the result of external violence, as falling astride a narrow object, or internal traumatism, as attempts to introduce instruments, or, in women, pressure of the child's

head during parturition, use of forceps, etc. Such injuries result in hemorrhage and extravasation of urine, and the tissues infiltrated are apt to suffer phlegmonous or gangrenous lesions with great rapidity. This is commonest in the male and may reach an extent which includes the lower anterior abdominal wall and the upper part of the thigh as well as the perineal tissues. This course of extravasated urine depends upon the

FIG. 112.



PAPILLOMA OF THE BLADDER. (*Delafield and Prudden.*) Fibro-cellular tissue, rich in vessels, invested with irregular layers of epithelium.

union posteriorly of the deep perineal fascia with the deep layer of the superficial fascia, "false passages" from the urethra usually opening into the space between. Fistulæ opening externally or into the ischio-rectal and other spaces may remain.

**Inflammations.**—Urethritis in the vast majority of cases is a specific disease produced by contact with infected persons;

the bacterial agent being the gonococcus. Simple catarrhal urethritis may occur, as the result of the passage of calculi, irritating drugs, and the presence of pyogenic organisms. Gonorrheal inflammation may be limited to the anterior portion of the urethra or travel through its whole extent and invade the bladder, prostatic glands, seminal vesicles and vas deferens; and in women, bladder, vagina, uterus and tubes are often involved. In the Fallopian tubes such an inflammation may become chronic and distend the parts with slow accumulation of pus. The inflammation is exudative, the epithelial cells desquamate in great numbers, pus-cells abound.

In the bodies of the cells, both epithelial and pus, at times in their nuclei, as well as free in the tissue and the discharge, the characteristic diplococci are found. They lie in twos and fours or irregular groups and are arranged with their flat or slightly concave surfaces opposed, with a narrow space between. They stain easily with anilin dyes and are decolorized with Gram's fluid; this fact and the difficulty of cultivating them are important characteristics. Pus organisms occur at first, but as the disease becomes chronic all forms of bacteria tend to disappear from the discharge, which becomes thin and colorless and lessens in amount. But in the crypts of the mucous glands along the urethra the gonococcus may linger for long periods, not very injurious for the patient but able to convey the infection to another.

Other parts attacked are the rectum, the conjunctiva and at times the joints (gonorrheal rheumatism); the diplococcus has been recovered from these places as well as from tendon sheaths, the glands of Bartholin and endocardial and peritoneal pus.

*Chronic urethritis* frequently follows the acute disease and the part most often involved is the posterior urethra; it spreads from here to the prostate and seminal vesicles in many cases. The discharge is thin, perhaps limited to a drop or two of glairy mucus noticed only in the morning. The part affected becomes

covered with little papillæ which at times are sensitive and bleed easily. A more serious sequel of urethritis is the formation of fibrous thickenings in the wall of the tube, either along the floor or in ring form. Such *strictures* probably begin as productive fibrosis about a small ulcer or a suppurating mucous gland, most commonly in the membranous portion, and the tendency is toward contraction of the tissue and stenosis or closure of the lumen. Such a mechanical obstacle produces hypertrophy of the bladder, dilatation of this viscus, the ureter and the renal pelvis, with decomposition of stagnant urine, or acute retention. Other complications are inflammation of the epididymis and the testicle, chronic prostatitis and vesiculitis, and impotence of various forms.

**Tumors** are not common in the urethra except when it is secondarily involved. Condylomata are observed about the meatus in the female, polypoid growths occur in either sex, carcinoma occurs with similar disease of the glans penis, the prostate, and the cervix uteri; but the urethra may escape even with extensive lesions of the neighboring parts.

*Tuberculosis* may invade the urethra as lupus from the skin or when the kidney and bladder are diseased.

*Syphilis* may occur as a chancre in or about the outer portion of the urethra.

# CHAPTER XIX.

## THE REPRODUCTIVE SYSTEM.

### Male Organs.

**Malformations.**—The penis may be absent or rudimentary, or in rare cases double. The prepuce may be absent, the urethra may open on the dorsum of the penis (*epispadias*) or on the under side (*hypospadias*); most cases of hermaphrodism are only severe degrees of such imperfect closure. The testicles may fail to descend into the scrotum (*cryptorchism*), and then be incapable of functionating; the inner genitals seldom present malformations.

**Injuries of Penis and Scrotum.**—Wounds of the penis cause hemorrhage, more marked when occurring during erection, and if the urethra is involved fistulæ or extravasation of urine may result. *Ganglion* of the penis is the name given to hard fibrous masses in the corpora cavernosa after injury with hemorrhage. Rupture or fracture of the penis may be due to violence during erection, the fibrous sheath of the organ is torn and severe bleeding follows. The penis may also suffer luxation, being crowded up under the abdominal integument by severe pressure, as of a wagon wheel. Permanent bending or twisting of the organ may result.

**Inflammation** of the glans is called *balanitis*, of the prepuce, *posthitis;* both usually come from lack of cleanliness or complicate *phimosis*, inability to retract the prepuce. *Paraphi-*

*mosis* results when a tight prepuce can not be drawn over the glans again after retraction, owing to edema of the tissue. Inflammation of the deeper structures of the penis seldom occurs.

*Ulcers.*—The commonest are chancre, the initial lesion of syphilis, and chancroids, and their usual seat is on the glans, behind the corona or elsewhere. Lupus may produce an indolent ulcer of the glans, carcinoma of the part often ulcerates, condylomata at times affect the glans, prepuce and scrotum.

**Tumors.**—Beside venereal warts, epithelioma affects the glans penis and the prepuce; it may be papillary and in any case ulcerates rapidly. It is commonest in late adult life.

Scrotal epithelioma (chimney sweeper's cancer) occurs as flat masses of induration in the skin with a tendency to ulcerate; it extends directly to the penis and through the lymphatics to the inguinal nodes. It affects workers in paraffin also.

In oriental countries the scrotum is at times the seat of elephantiasis, enormously enlarged, hanging nearly to the knees of the patient, and retraction of the penis within the leathery tissues leaves a funnel-shaped opening through which the urine discharges; fissures and ulcers are common in the swollen skin. In some cases the lymph spaces of the part are dilated and contain numbers of filaria.

## Testes.

*Hydrocele*, or dropsy of the tunica vaginalis, may occur with general edema, or, when the way to the peritoneum is open, ascitic fluid fills the serous sac of the scrotum also; a hydrocele of the cord also occurs. Injuries to the testis are sometimes followed by serous collections in the sac; epididymitis may be complicated by the same. In distinction to these acute cases of hydrocele, where the fluid rapidly accumulates and may be serous or mixed with blood and pus, chronic hydrocele grows slowly, the fluid is clear, and large amounts may collect and return after tapping. Papillary outgrowths from the epididymis

(*periorchitis prolifera*) and testis may develop, and these may separate after lime salts are deposited in them and lie as free bodies in the cavity. Filaria cause a kind of hydrocele in which the fluid is milky (*galactocele*).

*Spermatocele* is the name given to a cystic tumor containing fluid and spermatozoa which develops near the head of the epididymis.

*Hematocele* is either a hemorrhage into the tissues of the scrotum (hematoma) or a collection of blood within the vaginal sac, as in scurvy or with acute hydrocele. Injuries usually cause extra-vaginal hematoma.

*Embolism* of the spermatic artery and thrombosis of the pampiniform plexus in rare cases lead to a rapid spontaneous gangrene of the testicle; interference with the vessels of the cord may lead to fatty degeneration or necrosis of the organ.

**Inflammation.**—*Orchitis* may be the result of injury to the testis or complicate gonorrhea; when the disease is limited to the epididymis it is called *epididymitis,* when the serous coat is especially involved it is called *periorchitis.* With small-pox and some other diseases, and in a "metastatic" form with mumps, inflammation of the testis is occasionally seen. The acute form is attended with great swelling, and owing to the firm tunica albuginea the part is hard and very painful. The disease may end in complete restoration, or suppuration may occur, and when the tunica albuginea is broken through a fungous condition of the testis results.

Chronic orchitis may follow the acute form or complicate syphilis. The inflammation is chiefly productive and reduces the size and destroys the function of the organ.

Atrophy of the testis occurs with loss of function and after operative procedures involving the spermatic cord.

**Tumors.**—The commonest benign neoplasms of the testis are fibroma, lipoma and myoma; chondroma occurs simply or combined with sarcoma. Sarcoma occurs in all its forms in the

testicle and the same tumor may present a different constitution in various parts, as also in the parotid gland. Carcinoma is usually of the encephaloid type and combinations with adenoma and chondroma have been described. Metastases are usually rapid in all the malignant forms of tumor, as well as extension to surrounding parts by direct invasion.

*Tuberculosis* often begins in the canals of the epididymis and from here affects the testis later. It is apt to invade the seminal vesicles and the prostate also, and may reach the kidney by way of the urinary tract or the lymphatics. The disease develops slowly and the caseous masses may reach a large size; fistulæ opening externally may form and discharge pus and broken-down material. The disease is usually secondary to pulmonary tuberculosis, though this may be clinically less serious than the genital disease, and the question of transmission during intercourse naturally suggests itself, especially during the early stages.

Leukemic and lepra nodules have been found in the testis but are not of pathological importance.

## Seminal Vesicles.

Acute **inflammation**, usually a sequel of gonorrhea, may be accompanied by imperfect erection, premature ejaculation, bloody semen, and pain during and after coitus. Chronic inflammation is rather common as the result of posterior urethritis and often causes nervous symptoms, neurasthenia and melancholy. The vesicles can be felt by rectal touch as swollen, tender and thickened cords, usually distended with fluid; on massage their contents is pressed into the urethra and passed with the urine. Under the microscope hyaline crescentic bodies, dead or imperfect spermatozoa and Charcot crystals may be found, or in many cases complete aspermia. The dilatation is due to inflammatory products about the entrance of the ducts into the prostatic tissue.

Tuberculosis complicating pulmonary disease frequently starts in the vesicles, the bacilli being excreted with the semen and attacking the vesicles while stored in them. From here the disease may spread to the other pelvic organs, or caseous abscesses may form and be discharged by the urethra and apparent recovery follow; vesical and renal tuberculosis result.

Primary tumors are very infrequent. Small retention cysts are rather common. Small concretions form at times from coagulated contents in which salts are deposited.

## Prostate.

Acute **inflammation** of the gland may complicate gonorrhea, and, from the rapid swelling induced, retention of urine may follow. From this form a suppurative inflammation of more the lobes. Injury to the prostatic urethra and suppuration in chronic character may develop, resulting in abscess in one of the pelvic tissue may also cause abscess of the gland; in pyemia emboli of pyogenic organisms produce numerous small foci of pus. As a rule prostatic abscess empties into the urethra; less often the limits of the capsule are passed and the pus burrows into the rectum or along it to the perineal surface. When the urethra is opened extravasation of urine into the pelvic tissues occurs. Phlebitis may occur in the prostatic plexus, and, if septic, emboli from here may produce general infection. The gonococcus may gain an entrance to the circulation in a similar way and cause malignant endocarditis.

*Concretions* in old age are very common in the prostate. They may be visible to the naked eye as small brownish granules scattered over the section. Under the microscope the older bodies are striated, concentrically and in radii, the rings corresponding to increases in size and the radii to drying. They stain with iodine, either blue or reddish-brown, or not at all. Deposits of lime salts often occur about these bodies.

*Atrophy* of the gland is a regular senile change, follows castration (at times), and results from fibrous contraction with degeneration of the glandular epithelium.

*Hypertrophy* occurs in middle age and later, and because of the mechanical conditions is of great clinical and pathological importance. Either the stroma or the glandular tissue may be involved and the three common forms arise as one of these predominates or the two coexist. Thus the hypertrophied organ may be small and hard, chiefly made up of fibrous tissue and muscular bundles, the glands compressed and their epithelium atrophic; or it may be large and soft, the glands dilated, often containing concretions, muscular fibers increased in size and number; or both pathological changes may exist.

The gland normally has but two lobes; when hypertrophied it may have four. Either lateral lobe or both may grow, or the posterior isthmus below the internal meatus may be the chief seat of the hypertrophy, rising like a round knob into the bladder and transformed into a "middle lobe" only as the result of a pathological process; a similar smaller isthmus of gland tissue, not always present, which arches over the meatus, may constitute a fourth imperfect (pathological) lobe.

With middle lobe hypertrophy the new growth acts as a ball valve and prevents expulsion of urine, increased pressure by the vesical and abdominal muscles only pressing the tumor more tightly against the meatus internus. One-sided hypertrophy distorts the prostatic urethra, when bilateral the passage is much narrowed; in any case the prostatic urethra is lengthened and more curved than normal. The results for the bladder are mechanical at first, with hypertrophy of the muscular trabeculæ, and at times saculation between them. Later, when residual urine accumulates and decomposes, and the compensatory power of the bladder is lost, the case becomes graver, fever, sweating and other general symptoms are added.

The gross appearance of the organ varies with the kind of hypertrophy, and its seat; the cut surface may be soft and pale

FIG. 113.


MIDDLE LOBE HYPERTROPHY. (*Stengel.*)

*A*, hypertrophied middle lobe; *B*, urethra. The muscular tissue of the wall is much hypertrophied.

in the large form or harder when chiefly fibrous. Here and there may be areas with concentric arrangement of fibers like vortices separated by interlacing bands, as if the gland were made up of many smaller ones tightly pressed together. The capsula propria and the investment derived from the recto-vesical fascia may have become blended so that they cannot be separated, with only traces of the plexus of veins normally between them; out of this thickened capsule the hypertrophied gland may at times be shelled with slight effort. Microscopically the appearances correspond to the tissue which is most abundant.

The cause of prostatic hypertrophy is probably long-continued congestion, kept up for years. This may be the result of masturbation, imperfect intercourse (coitus reservatus), habitual excitement of the organ, without the normal relief of the functional hyperemia consequent on normal ejaculation, extension of chronic inflammation from the posterior urethra, and varicose conditions of the veins with impeded return.

**Tumors.**—Both sarcoma and carcinoma are very rare in the prostate, either as primary or as secondary tumors. Tuberculosis almost always occurs with other genito-urinary forms of the disease and requires no special discussion.

## Cowper's Gland.

In the course of gonorrhea the gland may become inflamed and suppurate; the pus may burrow and leave a fistula communicating with the urethra. When the duct is stenosed a retention cyst occurs, and with chronic inflammation fibrous induration is the common result.

## Female Organs.

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### Vulva.

**Malformations** are not of great pathological importance with the exception of atresia, partial or complete, and unusual

forms of the hymen which may have a legal interest; this membrane may be absent, or fimbriated, or a narrow ring of tissue with a wide lumen, or imperforate.

**Injuries.**—The most important are those received during parturition. These are chiefly pressure effects, which may produce sloughing of the labia, hematoma in one or both, perhaps extending into the vagina, and tears of the posterior commissure which may extend through the entire perineal body into the rectum. Slight tears usually heal rapidly in the absence of infection. Contusions may cause inflammation of the labia and of Skene's or Bartholin's gland, with abscess formation.

*Hyperemia* may be passive and accompanied with edema in pregnancy and hydremic conditions. Acute congestion occurs with various skin eruptions and with more extensive inflammation. Acute vulvitis may follow injury during attempted coitus, irritation from scratching (with pruritus), and in children thread worms leave the rectum, especially at night, and irritate the parts. The usual symptoms of redness, swelling and increased secretion follow. Gonorrhea may produce such an external condition and often the gland of Bartholin on either side is also involved and suppurates. Diphtheritic and phlegmonous inflammation occur at times, the last may result from pus burrowing from distant parts.

*Ulcers* on the vulva may be found with the above lesions, and in syphilitic patients both chancroids, often multiple, and chancres occur here. Gangrene may follow severe injury or in the cachectic occur spontaneously; a line of demarcation may form and the process heal with large contracting scars, but the probable course is to a fatal ending.

**Tumors.**—Soft fibroma and myoma sometimes occur on the labium majus or about the urethral opening, and reach a large size, usually pedicled and covered by thinned non-adherent skin. Lipoma and chondroma have been observed. Papillomata are far more common, in the form of broad or acuminate

condyloma, with syphilis; a non-specific form, of small size but extremely sensitive, develops in the meatus and is known as urethral caruncle. Carcinoma is rare but may develop from the clitoris, the labium minus or the epithelium of Bartholin's gland. It may extend in any direction and soon breaks down and ulcerates.

Tuberculosis occurs as lupus, with slow progress by ulceration while older parts cicatrize imperfectly.

## Vagina.

**Malformation.**—Atresia may occur at the hymen or elsewhere in the canal; it may not be discovered till menstruation begins and the monthly discharge distends the canal (*hematocolpos*). The vagina may be imperforate for its whole length, only a fibrous cord occupying its main axis, or it may be of normal size but divided by a septum; in the latter case the uterus is also double as a rule.

*Dislocation* of the canal usually follows rupture of the perineum or uterine displacements or both combined. Slight degrees of vaginal prolapse may arise from looseness of the attachments of either wall; the anterior wall is more often involved and may drag down the uterus with it. When this attains a marked development the bladder follows and the condition is known as *vaginal cystocele;* the name *phantom tumor* is also used, for the apparent tumor is easily replaced on change of position or by the examining finger. When the posterior wall and the anterior rectal prolapse it is called *vaginal rectocele.* With complete prolapse of the uterus both walls may be dragged out and their surface in time become dry and leathery, resembling epidermis.

**Wounds** of the vagina may arise from foreign bodies, violent coitus with great disparity of the parts, injuries during parturition from the head or obstetric instruments. Perineal rupture if complete also involves the vagina. Slight wounds

often heal quickly unless infected; then suppuration may occur and reach the deeper tissue, and the scars may make a partial or a complete stricture of the canal. Another result of injuries is the formation of *fistulae,* which may join bladder, vagina and rectum and involve the uterus and the pelvic tissues also. The lumen of the fistula may be very fine or large enough to permit the passage of urine and feces; severe inflammation and even gangrene may result; spontaneous healing is seldom secured.

**Inflammation.**—Acute *vaginitis* (or *colpitis*) may be a mild and temporary catarrhal inflammation, due to hot douches, mechanical irritation and, in children especially, the presence of oxyuris. The severe attacks may usually be referred to gonorrheal infection. The mucous membrane is then swollen, hyperemic, covered with a muco-purulent discharge, and the urethra usually shares in the process; shallow ulceration is common. A destructive vaginitis with necrosis of the epithelium and formation of a pseudo-membrane occurs in cachectic patients with pyemia, variola and other infectious diseases; it may accompany true diphtheria of the pharynx but commonly is quite distinct. The lesion ends in recovery with large scar formation and contraction, or in phlegmonous and gangrenous destruction of the tissues.

Chronic catarrhal vaginitis is usually known from the copious discharge as fluor albus or "the whites." The discharge is yellow or creamy, thick and purulent, or thinner and acrid, acid in reaction, at times greenish; the cervical canal is commonly involved also. In other cases the mucous membrane is dry and thickened, with almost no excretion.

**Tumors.**—Fibroma develops in the vagina as polypoid tumors or fibrous or fibro-myomatous type and also as acuminate condylomata. Sarcoma is uncommon. Carcinoma may occur as flat or papillary epithelioma, commonly in the upper portion of the canal, and at times develops into a large cauliflower mass; secondarily the vagina is usually involved with uterine cancer

of the cervical region and with similar disease of the anterior rectal wall.

Tuberculosis may appear either as lupus or as scattered ulcers, the former extending from the skin and the latter from the uterus. Syphilitic ulcers of all varieties may be found in the vagina.

## Uterus.

**Malformation.**—Imperfect development of Müller's ducts results in absent or rudimentary uterus or vagina, or both. A very small uterus is termed infantile or fetal and is remarkable for the disproportion between body and cervix, the latter forming most of the organ; the ovaries also may be lacking or undeveloped. The adjacent walls of the Müllerian ducts, which disappear normally leaving but one cavity in the genital canal, may persist more or less completely and give rise to the bicorn and bipartite uterus and the septum may divide the vagina also into two canals. Atresia of the cervix may lead to accumulation of menstrual blood (hematometra), or of muco-serum (hydrometra); inflammation and suppuration may follow.

**Displacements.**—The form and anatomical relations of the uterus both permit various displacements and make their results serious. When the organ moves as a whole, without alteration in its proper form, it is called *version,* of which the most important are anteversion, retroversion and lateral version. The effects are chiefly mechanical, from pressure on bladder and rectum or dragging on ligaments, and are less severe than in flexion. When the uterus suffers a bending in itself the condition is called *flexion,* and the degrees correspond to those of version, ante-, retro- and lateral flexion. The results are chiefly due to consequent narrowing of the uterine lumen, difficult menstruation and retained flow. The condition may be caused by pressure from above, as of the clothes, contraction of inflammatory adhesions and other external influences, and, in an imperfectly restored uterus after childbirth, subinvolu-

tion, loss of tone in its walls, and weight and congestion of the fundus may precede the condition. Entire movement of the organ upward has but little importance; the contrary condition. *prolapsus uteri,* is observed when the inferior support is lessened and the vulva patulous, as after rupture of the perineum. Three grades of this condition are distinguished, simple descent, the uterus not leaving the pelvis; partial prolapse, the organ being out of the pelvis but not entirely; complete prolapse, the uterus protruding from the vulva, and with it the vaginal walls and inside them the vesical and rectal walls.

*Inversion* of the uterus occurs after labor or with submucous polyps of large size, the traction turning it inside out more or less completely; this may be associated with prolapse.

*Rupture* of the uterus may result from accumulation of fluid within it, and thinning and necrosis of its wall, but this is very unusual. The accident more often takes place in the pregnant organ, and here there may be predisposing conditions, as malignant disease, destroying the muscular wall. Other cases result from convulsive efforts at expulsion of the fetus, disproportion between uterus and child, pregnancy in one half of a double uterus. The tear in the uterine wall is most often in the region of the cervix or just above it and proceeds from within outward; tears starting on the peritoneal surface are practically unknown. The depth of the injury may be less than the thickness of the wall (incomplete rupture), or pass entirely through it and not involve the serous surface, or include this and other parts also, as bladder and rectum. Copious hemorrhage into the peritoneum may be immediately fatal and with it the fetus and its envelopes may leave the uterus and be found in the clot. In very favorable cases, with but little bleeding, peritonitis may close in the fetus, adhesions may form, and purulent softening open a way for the escape of the dead fetus through the intestine. In any case the termination is usually fatal, from shock and bleeding, peritonitis or chronic suppuration.

Tears spontaneously produced usually lie in the direction of the long axis of the uterus, in or near the cervix; if caused by version or other obstetric procedure they may be oblique, transverse, and in other parts of the organ. Slight injuries of this kind usually heal quickly in the absence of infection. Other perforations, as from a curette (and the septic uterus as after abortions is very easily perforated) usually occur in the fundus and make small linear or branched openings on the peritoneal surface, with inflamed or necrotic edges, the wound widening toward the mucous surface.

**Circulatory Disorders.**—*Hyperemia* of the uterus occurs normally in a cycle of about twenty-eight days; death during menstruation leaves the mucous membrane swollen and congested, its upper layers degenerated or lost. Menstruation is associated with serous swelling of the mucosa and separation of its elements, round-cell increase between the glands, and increase in the length of the tubular glands. The swelling subsides rapidly with cessation of bleeding from the dilated capillaries, the upper layer of mucous membrane is exfoliated and the glands become spiral again. When the entire lining of the uterus, as a cast of its cavity, is extruded at menstruation, with pain and uterine contractions, the anomaly is known as *membranous dysmenorrhea*. The cause is usually an inflammation of the mucosa (exfoliative endometritis). The membrane is made up of uterine glands held together by very cellular connective tissue holding red cells in its meshes; in other cases the membrane consists chiefly of fibrin and blood-cells.

Certain infectious diseases, blood states and local conditions may cause uterine *hemorrhage* apart from menstruation; among these are cholera and small-pox, scurvy, and tumors. Hemorrhage in the tissues about the uterus may occur in the peritoneum (Douglas' pouch) or in the tissues, as of the broad ligament; the usual causes are menstrual flow from the tubes, rupture of extra-uterine pregnancy, rupture of a varicose vein or of newly formed vessels in adhesions, and injuries during par-

turition. The blood may form a large hematoma and in favorable cases is absorbed or encapsuled; in other cases inflammation occurs. The blood may escape through rectum or vagina after softening of their walls, or necrosis of the tissues may end fatally.

**Inflammation.**—The part of the organ attacked may be the serous coat (*perimetritis*), the subperitoneal tissue adjacent (*parametritis*) the wall of the organ (*metritis*) or the mucous surface (*endometritis*).

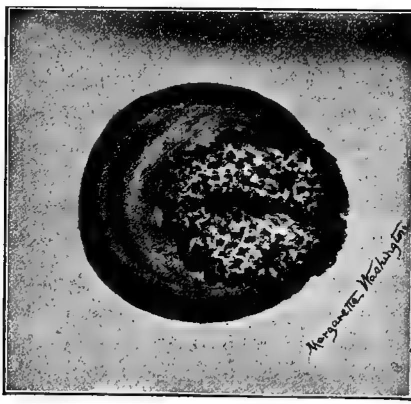
In the non-pregnant uterus *perimetritis* is usually either acute and part of a general pelvic peritonitis, or chronic and associated with other inflammations; either may cause fibrinous exudate with adhesions or pus formation. Such adhesions are almost constant with various tumors of the uterus. *Parametritis* is usually an acute inflammation of the cellular pelvic tissue about the uterus, and occurs with metritis and endometritis. Of these two forms many slight attacks may occur at variable periods and the pelvic contents may be firmly fastened together and to loops of intestine, the omentum, etc.

*Metritis* seldom occurs in the acute form except in connection with puerperal conditions. It may follow gonorrheal and other infection with marked lesions of the mucosa. Chronic metritis results from chronic congestion, subinvolution and displacement and is partly a fibrous and partly a muscular hyperplasia. The entire organ may be involved, but often the condition is limited to the inferior zone of the organ.

*Acute endometritis* is uncommon but may follow injury, or pyogenic and gonorrheal infection of the mucosa. It may be limited to the cervix (endocervicitis) or invade the fundus also. As a complication with infectious disease it ocurs in typhoid and scarlet fevers. The mucous membrane is swollen, congested, loosened in its attachment, hemorrhagic and covered with muco-purulent exudate; severe necrosis of the mucosa gives rise to a diphtheritic form.

*Chronic endometritis* follows the acute disease or results from anemic and chlorotic malnutrition of the part or irritation by polypoid and other tumors. The mucous membrane is thickened and congested, its glands are hyperplastic and irregularly dilated and the stroma may also show hyperplastic changes; with the progress of the disease an atrophic stage is reached when the glands disappear and the stroma becomes indurated. This process in the cervix results in retention cysts of the glands, forming the ovules of Naboth. The discharge of chronic

FIG. 114.



LACERATION AND EROSION OF THE CERVIX. (*Stengel.*)

catarrhal endometritis may be purulent, at times mixed with blood, but in many cases it is thin and colorless. The inflammation may extend into the tubes, atresia of the cervix may result from it, and membranous dysmenorrhea is another commonly associated condition. Ulcers in the fundus sometimes accompany the process; on the cervix they are extremely common and are known as erosions. The granulation tissue may be so exuberant as to close the cervical canal. Such erosions are common after laceration of the part. More superficial lesions

occur from loss of the squamous epithelium of the part; its place may be taken by cylindrical cells.

*Puerperal Metritis.*—The recently emptied uterus presents a natural wound; this and other traumatism of any part of the parturient canal, even very shallow tears in the mucous membrane of the lower vagina, may be the entering point for the infecting organisms. Deaths from childbed fever have steadily declined in some hospitals when the nurses have been forbidden to make digital examinations of the vagina before and during labor; further decrease has followed extension of the order to the visiting students, and when nobody was excepted the mortality for long periods has been nil. Such facts, and the frequency of the infection in the practice of certain physicians and midwives, suggest the source of the infection and the difficulty of avoiding it altogether, even with care. The organisms found have been strepto- and staphylococci, alone or together, the gonococcus, b. aërogenes, b. coli and b. tetanus. As a rule no part of the organ escapes, and the pelvic tissues may also be inflamed; the general condition may be that of septicemia, but local septic phlebitis often results in embolic abscess in various organs (pyemic form). The veins involved may be the sinuses at the placental attachment, and when the disease arises in consequence of putrefaction of retained placenta this is the natural source of general infection. A phlegmonous form occurs with lymphangitis of the organ, abscesses forming in the wall of the fundus at the attachment of the tubes, or in the cervix, in the broad ligament, and the cellular spaces of the pelvis. Suppurative peritonitis develops early and is usually fatal.

*Atrophy* of the entire uterus occurs as a senile change, with obliterating arteritis of the vessels of the part; it may occur early in life after removal of the ovaries. Hypertrophy occurs with chronic metritis. Fatty degeneration may result from poisons (phosphorus) or accompany infectious disease or pres-

sure from tumors (intramural fibromata). Amyloid changes are very infrequent.

*Tuberculosis* of the uterine mucosa may arise from extension of a tubal lesion. The entire mucosa may be thickened and caseous, with large losses of substance from softening, or a few miliary tubercles may be found here and there in the membrane; the disease usually accompanies other genital tuberculosis and similar disease of the peritoneum.

**Tumors.**—Polypi result from localized submucous hyperplasia and hang in the uterine cavity of the vagina as small red and pedicled tumors. They may be mucous, cavernous or glandular, and are of importance from the accompanying hemorrhages.

*Fibromata* are the commonest tumors of the uterus. They occur under the serous or the mucous coat or in the substance of the organ, and hence are called subperitoneal, submucous or intramural. They may be single or multiple and an intramural tumor may become either subserous or submucous; the latter varieties are often provided with a pedicle. In size they vary from a few millimeters to many centimeters in diameter, though the large tumors weighing several kilograms are seldom seen at present.

The consistence of the tumor varies with the proportion of fibrous tissue, but they are often very hard, sharply circumscribed by a capsule out of which they may be lifted, and poorly supplied with blood-vessels. Degeneration is common in their middle portions and lime salts may be deposited in them, on the surface or diffusely. When a pedicled subserous fibroma becomes twisted on its pedicle it may become necrotic and cause suppurative peritonitis. Lipoma, myxoma and sarcoma may be combined with the original tumor.

Microscopically these tumors usually contain some muscular fibers, often so many that they are called fibromyomata; these cells are of large size and provided with large nuclei. An apparent concentric arrangement can be made out by which the

muscular and fibrous elements are disposed about a dilated capillary. Occasionally the capillaries are so large and numerous as to form telangiectatic and cavernous myomata.

The effects of uterine fibroma comprise the results of pressure on adjacent parts, displacements of the uterus, bleeding from the congested mucosa and degeneration of their tissue. The submucous forms may simulate inversion of the uterus, and are exposed to various injuries, with the danger of hemorrhage and inflammation.

*Sarcoma* may develop from fibro-myomata (myoma sarcomatodes), and is commonly of the spindle-celled variety; or it may start in the deeper layers of the mucosa and form polypoid vascular tumors, commonly round-celled. Adeno-sarcoma and angio-sarcoma may develop from the endometrium. A peculiar papillary edematous sarcoma sometimes occurs in the cervix during early life. Its nature is very malignant and the microscopic structure complex, including round and stellate cells, giant cells, muscle and cartilage, in a myxomatous and edematous matrix.

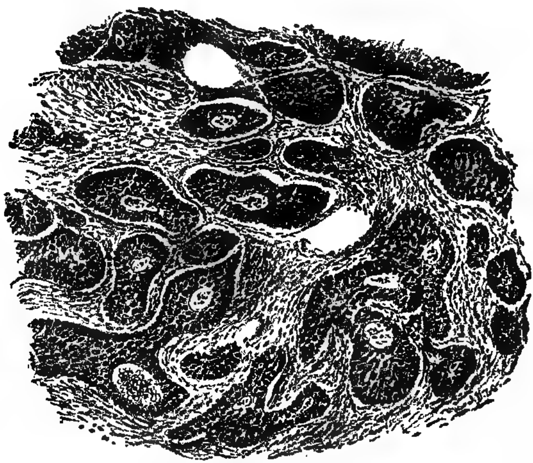
Epithelial tumors of the uterus may follow the type of the squamous cells of the cervix (vaginal aspect) or the cylindrical glandular cells. It is not uncommon for these tumors to begin as a benign growth and pass over later into a true carcinoma.

*Papilloma* forms relatively small and hard tumors, often multiple, on the portio vaginalis; the surface of the tumor is covered by many layers of flat epithelia.

*Adenoma* occurs as hypertrophies of the uterine mucosa after chronic inflammation, and as polyps. A malignant form takes its origin in the mucosa of the fundus and is distinguished from the simple glandular hyperplasia by the tendency of the atypical glands to invade the muscle of the organ. In tumors of this variety the epithelium often grows with great rapidity, the acini of the glandular structure are broken through and the transition to carcinoma is complete (Adenoma destruens), Pt. I., p. 166.

*Carcinoma* is the commonest malignant tumor of the uterus and its usual seat is the portio vaginalis. It begins on the inner surface of one of the cervical lips as an area of firm induration, not well circumscribed from the surrounding healthy tissue. The mucosa thickens and is adherent to the layers beneath. The disease progresses till it invades the vault of the vagina and rapidly breaks down. The ureters and bladder are sooner or

FIG. 115.



CARCINOMA OF THE CERVIX. (*Stengel.*)
Cell nests in a fibrous stroma with suggestions of a lumen in the former—Adeno-carcinoma.

later involved, the rectum may be opened, and the entrance of urine and feces hastens the destructive action of the cancerous ulcerations. Metastasis to the inguinal and lumbar nodes and to the liver are common; the fundus uteri is not involved or late in the disease.

*Epithelioma* of the cervix differs from benign papilloma in the rapidity of its growth, the softness of its tissue and the formation of but one broadly based tumor. The growth of the

new epithelial tissue occurs in two directions at once, into the muscular fibers of the cervix and out into the vagina as an increasing cauliflower growth. Both these varieties of malignant neoplasm lead to profuse hemorrhage; the epithelioma does not ulcerate nor invade surrounding parts so rapidly.

Carcinoma of the body of the uterus may be of the flat-celled type, in women of advanced age, in whom the epithelium of the fundus has become squamous after chronic inflammation; otherwise the tumor is cylindrical celled, and resembles malignant adenoma in many cases.

*Cysts* of the uterus are rare; they arise from softening in fibro-myomata or are small retention cysts of the mucous glands, or occasionally dermoid. Cystic parasites have been encountered (echinococcus).

## Ovaries and Tubes.

Either or both organs and ducts may be absent; hypoplasia is more common; occasional displacement occurs, as into a labium majus.

Acquired displacement of the ovary is common with uterine version and flexion; the ovary frequently lies in Douglas' pouch and has been found in crural and other hernias.

*Congestion* is normal before ovulation; passive congestion may be part of a general stasis.

*Hemorrhage* into the follicle follows extrusion of the ovum and forms the corpus luteum of menstruation, which soon organizes and disappears, all but a small scar on the surface of the ovary. The corpus luteum of pregnancy is larger, persists till the middle or end of pregnancy, has a gelatinous, semi-transparent contents, seldom contains blood, and has a luteal border which is very much broader.

**Inflammation** accompanies ovarian tumors, extension of salpingitis and peritonitis. In the puerperal form, as in the first

mentioned, one or both ovaries may be affected and the tube may also take part or escape for a time. The inflamed ovary is swollen, hyperemic and succulent or grayish-yellow in color. The process may resolve or lead to abscess formation and peritonitis. Adhesions form with surrounding viscera and remain as firm bands after the inflammation ceases.

**Tumors.**—The most important pathological condition of the ovary is furnished by its neoplasms. They are very often cystic.

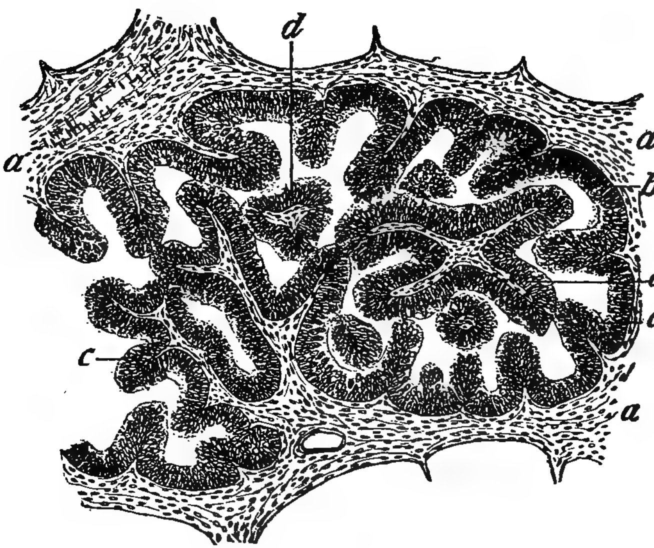
*Fibroma* occurs as simple, sometimes of large size, or as fibro-myoma resembling the uterine tumors, or as fibro-sarcoma. It probably takes its origin in the fibrous scars left after healing of corpora lutea. *Sarcoma* is most often either spindle-celled or combined with fibroma; round-celled forms, angio-sarcoma and myxo-sarcoma also occur.

*Cystic tumors* may develop in the follicles (hydrops of the Graafian follicle) and occur singly or multiple, in the young but more frequently in older patients. They are small or of medium size, seldom much larger than the fist, and the interior is lined by a single layer of flattened epithelium. They contain clear fluid which may be thin or jelly-like, or, with hemorrhages, dark.

*Myxoid cysts* (colloid) differ from the former in having thicker walls, more copious vascular supply, and a differently arranged epithelium. The so-called glandular form (adenocystoma) is clothed internally with cylindrical epithelia in constant development, arranged in acini and resting on a vascular basement membrane. They may be multilocular or contain imperfect septa, or the proportion of the wall may be so great that the cavities appear as simple fissures and spaces in it, though clothed with epithelium. The contents of the cyst is thick and gelatinous, though in old tumors it may be serous; it contains pseudo-mucin, which forms a slimy solution in water and is not precipitated by acetic acid.

The *papillary form* of ovarian cysts is often observed in both organs at once. It has a layer of ciliated epithelium and is arranged in papillary projections on its inner surface; secondary cysts are less common, hemorrhage is more frequent, concentric masses of calcium carbonate (psammoma bodies) are more com-

FIG. 116.




PAPILLARY CYSTOMA OF THE OVARY. (*Ziegler.*)

*a*, stroma; *b*, stratified epithelium; *c*, longitudinal sections of papillary out- outgrowths; *d*, transverse sections.

mon both in the stroma and the epithelial collections, than in the glandular form; pseudo-mucin occurs but less copiously. The *glandular form* may arise from Pflüger's glands (remnants of the fetal mesothelium) or hyperplasia of the Graafian epithelium; they are less malignant than the papillary tumors. The latter arise from parovarian inclusions in the ovary or

from the Graafian follicles. The genesis of neither form is accurately determined. Papillary tumors may form a metastasis to the peritoneum or become carcinomatous.

*Dermoid cysts* of the ovary are either loosely attached by a pedicle or are larger and supplant the ovarian tissue. They are common and affect one ovary. They may be teratomata, made up of all three embryonic layers and their products, or more strictly "dermoid," like similar tumors of other parts. They contain hair, fat, cholesterin, sweat glands and teeth in the simpler forms, and bone cartilage, gland tissues, suggestions of organs of special sense (as the eye) and tissues resembling that of the nervous system in the more complex. For these tumors the name *fetus in fetu* is perhaps appropriate, though they have been explained as parthenogenetic developments from unfertilized ova.

*Carcinoma* of the ovary may develop in the walls of a glandular cystoma or start in the epithelium of the follicles; it rapidly invades the peritoneum in some cases.

## The Fallopian Tubes.

Congenital or acquired *stenosis* of the tubes may be partial or complete; common causes of the latter form are inflammatory adhesions, which compress one tube or keep it sharply bent, and tumors in the uterine wall. The result of closure of the part is usually the collection of muco-serous fluid in it (*hydrosalpinx, hydrops tubae*). The distention often proceeds from the outer to the uterine end and dilates the part irregularly. The internal pressure drags the muscle fibers apart and causes atrophy of them and of the mucosa; the fimbriated end is usually inverted. The weight of the swollen tube may cause lateral and other displacements of the uterus. The fluid, which is clear and thin in most cases, may escape by way of the uterus.

Hyperemia occurs with peritonitis and metritis or is passive with impeded flow in the vena cava. Slight hemorrhages may occur from the tube during menstrual congestion, emptying into the peritoneal cavity or the uterus. The most copious tubal hemorrhage is associated with pregnancy and rupture in the part.

**Inflammation.**—*Salpingitis* may be catarrhal and either acute or chronic; it is usually associated with similar diseases of the uterus. Localized inflammatory adhesions often result between the tubes and the bladder, ovary or intestine.

*Suppurative salpingitis* is the result of gonorrheal or puerperal infection; in the former the infection may be mixed, the mucosa is hyperemic and thickened, the epithelia desquamate and the contents of the tube become purulent. If the pus is not emptied it may remain for a long time (pyosalpinx) and again become active or rupture as the result of later injury. In the puerperal form the inflammation may begin at either end, both may be closed by the edema and inflammatory exudate, and the fimbriæ inverted; the suppuration may involve the entire thickness of the wall and lead to rupture, either into the general peritoneal cavity, a hollow viscus, or an artificial space formed by adhesions. As in the other form, the pus may remain in the tube and thicken, mineral matter may deposit in it. Combinations of salpingitis and pelvic peritonitis and cellulitis are common and the abscess thus formed may be of large size. The pyogenic agent is often the streptococcus, but the pus may be sterile.

**Tumors.**—Benign forms are not of great importance nor of large size; they may be fibroma, myoma, lipoma and papilloma, usually projecting into the tube but also presenting externally in some cases. Malignant tumors occur as the result of extension from the uterus and ovary.

*Tuberculosis* is not infrequent as a secondary lesion, with peritoneal and pulmonary affections, far less frequently with other genital tuberculosis. The disease begins at the fimbriated

end of the tube and proceeds toward and into the uterus, miliary tubercles occurring in both serous and mucous coats. Chronic forms are accompanied by the usual infiltration and caseous softening. The tube is usually adherent to neighboring organs, swollen, thickened and distended, its mucous coat destroyed in places by caseous ulcers and the lumen filled with cheesy and purulent material. Primary tuberculosis of the tube does occur, often on a basis of gonorrheal inflammation. Both tubes are commonly involved in either form.

## Mammary Gland.

**Malformation.**—With imperfect sexual development the breast may be absent or hypoplastic; the gland may be normal but lacking a nipple; supernumerary mammæ (polymastia) occur on the abdomen, back, thigh and elsewhere, in either sex, and the extra breast may have or lack a nipple; they at times functionate.

A certain amount of congestion is very apt to occur with menstruation and the close sympathy between the organ and the genital system is shown also by premature development and function of the breast with premature sexual maturity, atrophy of the gland with cessation of sexual life, pain and swelling when the uterus is the seat of inflammation and other lesions. Other causes of hyperemia of the breast are injury and inflammation. Hemorrhage occurs after severe contusions and may be situated in the connective tissue or in the gland tissue; if the bleeding takes place into a lacteal duct it may dilate it and appear at the nipple. The extravasation may become surrounded by fibrous tissue (blood cyst). With tumors of the part bleeding is usual, both in the neoplasm and on the ulcerated surface.

**Inflammation** seldom occurs in the mammary gland except with puerperal infection, but the normal swelling of the gland which occurs at puberty in both sexes may pass into a mastitis,

with swelling of the axillary nodes. Lesions of the ribs (caries) and the skin (erysipelas) may result in the same. Puerperal mastitis may be conveyed through the blood current (metastatic form) or enter the gland through the milk channels, and slight injuries to the nipple during suckling predispose to the latter form. The entire organ may be involved or only a section of it; the usual result is abscess formation and when the inflammation exceeds the limits of the organ paramastitis also occurs. The abscess, which may be single or multiple, may open into the milk channels, the tissues about the gland or externally (fistula formation). The abscess cavity slowly fills and heals by granulation from the sides. Rupture into the pleura with fatal empyema is very unusual.

*Hyperplasia* of all the elements of the gland may lead to enormous development of one or both breasts (*giganto-mastia*), without effect on the general health, but, if functionating, to corresponding production of (normal) milk. A hyperplasia limited to the fibrous tissue of the organ (diffuse fibroma) may preserve or reduce the size of the breast, causing extreme hardness of the part and cysts of the milk channels. A circumscribed fibrosis occurs and may return after operative removal.

**Tumors.**—*Myxoma* may develop from the connective tissue of the organ as a diffuse tumor; the epithelium usually atrophies and disappears. If the neoplasm follows the milk ducts it is called intracanalicular myxoma.

*Sarcoma* of the breast may be diffuse or nodular. In the diffuse form the gland rapidly enlarges, usually but one, the process involves the skin and other tissues beyond, the gland becomes immovable and ulceration begins on the surface. On section parts of the tumor resemble fibrous tissue, other parts are myxomatous, others are soft and vascular; cysts from degenerative softening and from dilatation of the ducts occur, often of small size and containing clear or bloody fluid. If the cysts are an important feature of the tumor and chiefly

from dilated natural cavities the name cysto-sarcoma is given to it. An unusual form of this tumor occurs when the sarcomatous process follows the milk ducts and distends them, the new tissue being covered by a layer of gland cells. The circumscribed sarcomata usually start in the ducts near the nipple and after a period of very slow growth become diffuse. Sarcoma starts in the adventitia of the ducts or the vessels or the interstitial fibrous tissue. Metastasis occurs through the blood-vessels and is not so pronounced a feature of the disease as in carcinoma.

*Adenoma* of the mamma is commonly combined with fibroma, lipoma, myxoma or sarcoma. It causes hyperplasia of the ducts and occurs chiefly as an encapsuled tumor, less often without being circumscribed. The epithelia of the neoplasm may be larger than normal but typically arranged in the acini, or with more rapid multiplication they fill the lumen and undergo degenerative changes.

*Carcinoma* of the breast is a frequent disease in women, between the years of 40 and 50, and apparently connected with the end of sexual life; the right breast is somewhat more frequently affected than the left. It occurs also in the male in about two per cent. of all cases. Injury is sometimes given as the preceding cause by the patient, but in many cases this is a coincidence, rendered important by the growth of a tumor later; in other cases a preceding inflammation seems to prepare the way for the neoplasm, or a benign tumor becomes carcinomatous (fibroma and adenoma). A special form known as Paget's disease begins as papillary dermatitis (eczema) of the nipple and its vicinity and carcinoma develops later in the same area; it has been claimed that the "eczema" is in itself a carcinomatosis of the epidermis.

All varieties of carcinoma and combinations with other forms, and degenerative changes in the tumor when formed, are encountered in the breast. They begin as hyperplasia of the epithelia in the acini of the gland (acinous form) or in

the larger ducts (tubular form), and at first strongly resemble a simple adenomatous process. But the cells soon become very numerous, lying in several layers on the membrana propria, and in form they differ from typical epithelia in proportion as the disease advances; the limiting membrane is soon broken through and for a time its spindle cells may be recognized in the now atypical acini. The masses of cells are arranged in sinuous columns and smaller series through the gland, lying in the distorted acini and between them and invading the adjacent structures, as the pectoral muscles and afterward the pleura and lung. These masses of cells in a loose communicating mesh work are separated by a stroma much infiltrated with round cells. In some forms the fibrous stroma increases steadily, contracts, and atrophies the epithelia, so that narrow spaces are left between its trabeculæ containing a few cells or their detritus. The usual degeneration observed is fatty, but myxomatous changes occur in either the connective tissue or the cell masses and calcareous deposit is common. Hemorrhage occurs in the softer forms, and, with ulceration, from the surface, but it is not so much a feature of the disease as in sarcoma.

The chief varieties are:

1. Carcinoma simplex, in which the disproportion between stroma and cells is not marked, the tumor is not so soft as the medullary nor so hard as the scirrhous, and is less malignant than the former and more than the latter.
2. Medullary carcinoma, rich in cells, rapid in growth, the section yields much "cancer juice," hemorrhage may occur, ulcerates quickly and extensively; inflammation may coexist with abscess formation (mastitis carcinomatosa); malignant.
3. Scirrhous carcinoma, made up chiefly of fibrous tissue, slow of growth and relatively not very malignant;

hard, little juice, nipple contracted to complete inversion; may ulcerate but ulcer also of chronic character.

4. Colloid or gelatinous carcinoma, by degeneration of either of the previous kinds; the change is often limited to but one portion of the tumor; rare form.
5. Cystic carcinoma, from dilatation of glandular acini, the contents thin or jelly-like or fatty; unusual variety.

Metastasis is common and may be extensive with mammary carcinoma, the lymphatics of the axilla and clavicular region being successively involved and distant parts like the bones (vertebræ, pelvis), and adjacent organs, as the liver, pleura and lungs, being secondarily attacked. A local "regional" invasion is spoken of when secondary nodules form in the skin and tissues near by with intervals between. Microscopic secondary nodules in the skin are very frequent and explain recurrence in the scar after operative removal of the growth.

A form of epithelioma of the surface of the breast, with rather slow destruction of the surface and a narrow progressing edge of epithelial neoplasm, may occur on the breast as on other parts. It is often called rodent ulcer because of its gross appearance and slight resemblance to a neoplasm.

*Cysts* may be the result of occlusion of a milk duct and retention of the secretion; they may be small and multiple or fewer and larger; the contained fluid may be milky or serous, or thick and caseous.

*Tuberculosis* of the breast occurs with general disease of this nature and is a possible source of transmission to infants, for the bacilli pass out with the milk. It usually appears as a localized and chronic lesion and the breast commonly loses its function and atrophies.

*Syphilis* seldom attacks the breast but gummatous formation and its scars may be found.

## APPENDIX TO CHAPTER XIX.—DISORDERS CONNECTED WITH PREGNANCY.

**Extra-uterine Pregnancy.**—When the ovum is impregnated at the ovary, after the follicle has burst, a so-called *ovarian pregnancy* may occur, but is one of the rarest forms of the condition. *Tubo-ovarian pregnancy* is somewhat more common, the developing embryo being in part covered by the tube, in which the placenta usually forms.

*Tubal pregnancy* results from bending and partial occlusion of the canal which hinders the impregnated ovum from reaching the uterus; it is more common than the former. The chorionic villi grow into the mucosa of the part and an imperfect placenta forms from its vessels; the site of the fetus may be at either end of the tube, and with any variety it is common for a partial formation of decidua to occur in the uterine cavity. The embryo may die early or reach the third month; at that time the tension usually ruptures the tube, with bleeding into the periteneum, which is worst when the placenta is torn, and danger of death from loss of blood or from peritonitis. When the embryo with its membranes leaves the tube it may form attachments to the peritoneum and be converted into a stony mass by the deposit of lime salts (lithopedion).

*Abdominal pregnancy* may be primary when the ovum settles on some part of the peritoneum and begins to develop without entering the tube; or secondary after exit from the ruptured tube.

**Lesions of the Fetal Envelopes and Placenta.**—Fleshy moles result from hemorrhage into the decidua, coagulation of the blood and degeneration of the tissues; adhesions between the fetal envelope and the placenta may form. The fetus dies and the mass is expelled or calcareous changes occur. Placental fragments which remain in the uterus may lead to formation of polypoid adenomatous growths; commonly after

abortion. A destructive placental polyp is due to the hyperplasia of the placental elements and the invasion of the uterine wall by round, spindle and large epithelial cells.

*Syncytioma malignum,* or malignant deciduoma, doubtless takes origin in a manner similar to the foregoing. These tumors contain two varieties of cells, large epithelioid elements which are polymorphic and seem to multiply without mitosis, and smaller polyhedral cells which contain glycogen and multiply by mitosis. The former are regarded as coming from the syncytium and are frequently grouped in large masses and meshwork with coagula between them; the others are derived from the chorionic villi and lie in masses between the first variety. Transitions between the two are common. Metastasis occurs through the blood current, in the lungs frequently, the liver and the genital organs, and in this respect the tumor resembles a sarcoma; its epithelial elements suggest relationship with carcinoma. It is best to regard it as a mixed tumor like other forms which start from fetal inclusions.

*Hydatid moles* develop from edematous chorionic villi with hypertrophy and myxomatous changes, or from active hyperplasia of these structures with similar degenerations. They occur in connection with general anemic conditions (nephritis, chlorosis), entail the death and destruction of the fetus, and usually resemble a bunch of grapes, little cystic clusters hanging together by a few pedicles. Microscopically they consist of epithelial cells covering edematous or mucoid connective tissue, with few cells and some free nuclei; necrotic and calcareous changes occur in them.

The placenta may be hypoplastic or hyperplastic; it may be inserted over or near or within the cervix (*placenta previa*); its form may vary from the usual round cake, and small supplementary placentas occur. The attachment of the cord may be at the margin and if wide and fan-like is called a velamentous insertion; the cord may be partially double and knots and twists are fairly common.

Hemorrhage into the placenta occurs, and if large may cause death and expulsion of the fetus; hemorrhage from the placenta is a dangerous complication of placenta previa. So-called "infarcts" in it may be due to coagulation necrosis during the later weeks of pregnancy; they are yellowish-white areas made up of fibrin and round cells with red blood-cells.

Inflammation of the placenta may be diffuse fibrosis or localized nodules; the new tissue is often arranged about the vessels. The entire placenta may be indurated and either loosened in its attachment to the uterus or more firmly fixed. Placentitis may be due to extension from endometritis.

*Tuberculosis* and *syphilis* may affect the placenta, the usual gross and microscopic lesions developing as in other tissues. A syphilitic taint is assumed in many cases of placentitis. Fatty and calcareous degeneration of the placenta may occur.

Many of these conditions lead to the death of the fetus at various periods of pregnancy. It may then be expelled, or remain in the uterus for a long time and undergo putrefactive changes, and as the result of these the mother may become septic.

# CHAPTER XX.

## THE NERVOUS SYSTEM.

THE histological and physiological unit of the nervous system is the nerve cell, or neuron. This is provided with processes, called dendrites, which branch dichotomously, and with a centrifugal prolongation called an axis cylinder, or axon, which is surrounded by the myelin sheath. Comparing the

FIG. 117.

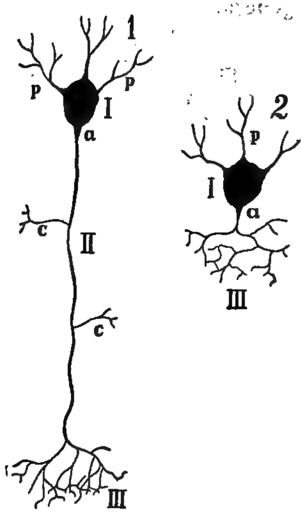



DIAGRAM OF TWO NEURONS. (*Obersteiner.*)

*I*, nerve cell; *p*, its protoplasmic processes; *a*, axis cylinder; *II*, nerve fiber, with collateral and terminal branches; *2*, a neuron of the second type, whose axis cylinder breaks up immediately into terminal branches.

nervous tissue with a gland, the parenchyma would be represented by the neuron with its processes, and the stroma by a peculiar tissue in which it lies, called the neuroglia. The latter is treated as connective tissue, but it must be remembered that it is derived from the ectoderm. The chief cells of the neuroglia are called "spider" and "mossy" cells.

The nerve cells have a cell body of spongioplasm, a nucleus and a nucleolus, and are classified by their reaction with a special stain (Nissl's) and by the size of the cell body. The following varieties are described:

1. Somatochrome cell, having a large cell body.
2. Karyochrome cell, with a nucleus as large as that of the somatochrome cell and but little cell body.
3. Cytochrome cell, with a nucleus of the size of a leucocyte and very little cell body.

Within the body of the somatochrome cells there are fine fibrillæ, and, arranged differently in the various kinds of somatochrome cells, a so-called "tigroid" substance which has strong affinities for methylene blue, thionin, neutral red and other stains. According to the arrangement of the tigroid material, the somatochrome cells are further distinguished as:

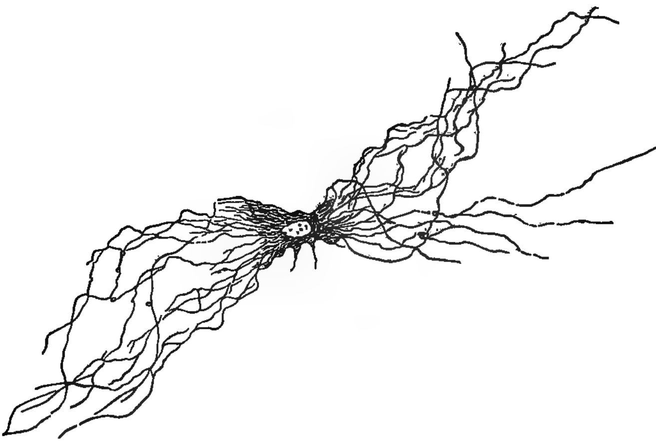
a. Arkyochrome cells, with the tigroid substance reticular.
b. Stichochrome cells, with the tigroid matter in more or less parallel striations.
c. Gryochrome cells, with granular tigroid substance.

Pigment occurs normally in the somatochrome cells from certain localities, as the substantia nigra and the locus ceruleus. In the spinal ganglion cells it appears about the sixth year, and a little later in the motor neurons. Where the pigment is found, commonly at the base of a large dendrite, the tigroid substance is lacking. Each nerve cell lies in a lymph space, which communicates with the perivascular spaces. As in other cells, but especially in neurons from their chemical complexity, which implies instability, and their high specialization, which means sensitiveness, nutritive disorders and toxic

influences produce rapid and marked degeneration. When this affects a neuron the axis cylinder is cut off from its trophic center, and undergoes degeneration, apparently throughout its extent. The myelin is converted into oval and globular masses, fat accumulates in the sheath and the dendrite is absorbed.

In the neuron the earliest pathological change is a cloudiness of the tigroid substance, called *tigrolysis,* and the nucleus

FIG. 118.



GLIA CELL FROM THE HUMAN CORD. (*Obersteiner.*)

becomes swollen and eccentric. Then the cell body presents vacuoles and becomes broken, leaving fragments of tigroid material about the irregular nucleus, and after a time this also becomes fragmented.

*Pyknosis* is another form of degeneration in neurons. The cell body becomes denser, shrinks, and stains so intensely with thionin that the nucleus may be obscured.

Other pathological changes affecting neurons are calcification and pigmentation.

The causes of lesions in the nerve cells include imperfect nutrition, high bodily temperature, poisons introduced from without, the toxins of infectious diseases, and certain bodily conditions, but the changes in the nerve cell are not characteristic of any special cause.

Just as certain neurons differ from others in their functions, so pathological influences spare one kind to attack another, and this is known as selective action. In tabes dorsalis, for example, the sensory neurons are diseased, and ergot produces a similar effect, while lead-poisoning involves special motor neurons as a rule. When special groups of neurons are diseased, from the selective action of some poison, the resulting lesion is called a systemic disease. The action of chronic poisons may be strongly predisposing, so that a slight injury may be followed by a nervous disease, and a good example of this is paralysis of an extremity in an alcoholic patient after a slight trauma, or delirium tremens developing with pneumonia, in both of which cases the toxic action of the alcohol is the real cause of the lesion.

When nerve cells degenerate there is always an apparent irritation of the stroma which causes it to proliferate. This is called a gliosis, and replaces nervous tissue by fibrous. When death occurs before the gliosis, there may be marked fatty changes, and as the fat is dissolved by alcohol and ether in hardening the tissue, the section may present many vacuoles.

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## THE CEREBRAL MEMBRANES. THE DURA MATER.

**Disorders of Circulation.**—Both active and passive *hyperemia* of the dura affect the layer nearest the cranial bones, which acts as their periosteum, more than other layers. Injury to the head, fractures, caries and syphilis of the cranium, are accompanied by congestion of the dura. Stasis affects the sinuses of the dura especially.

*Thrombosis* of the sinuses may follow injury, adjacent inflammation (as of the middle ear), and infectious diseases. It may result in stasis and softening in the brain, cerebral abscess, cardiac or pulmonary embolism, and such disturbance of cerebral functions as to end fatally.

*Hemorrhage* between the dura and the bones is seen with severe contusion, both with and without actual fracture. The amount of blood may be so great as to strip the dura from the bone for a large extent, and by its inward projection it may cause severe compression. The collection is called an internal hematoma. Small multiple hemorrhages in the substance of the dura may be found after death from asphyxia.

**Inflammation.**—Hemorrhagic pachymeningitis occurs most frequently in the area supplied by the middle meningeal artery. A delicate red or brownish film, continuous or interrupted, forms on the inner side of the membrane, and although loosely connected with the finer vessels, it may be easily stripped off. It is made of soft connective tissue, many thin walled vessels, occasional round and spindle cells, and groups of red cells and crystals of hematoidin. The dura beneath it is congested but smooth. Such mild degrees of the lesion are common in aged and alcoholic patients and in certain forms of insanity. Any part of the dura may be involved.

In more pronounced cases the false membrane consists of several layers, in varying conditions of organization and often including large hemorrhages; this is sometimes called hematoma of the dura. Firm fibrous tissue and more recent cellular tissue are found in such masses, with partly organized clot and many delicate new vessels. The clinical symptoms, of irritation and pressure alternating with remissions, correspond with the anatomical conditions, as new bleedings occur followed by organization.

The initial stage of such chronic meningitis is doubtless hemorrhagic (diapedesis) rather than inflammatory. Repetition of the bleeding may cause death by apoplexy, when large and

sudden. The blood usually collects between the older and newer layers of the false membrane, so that the latter, near the pia, forms a covering for it. The blood may be partly absorbed and its place taken by serum, forming hygroma of the dura.

FIG. 119.

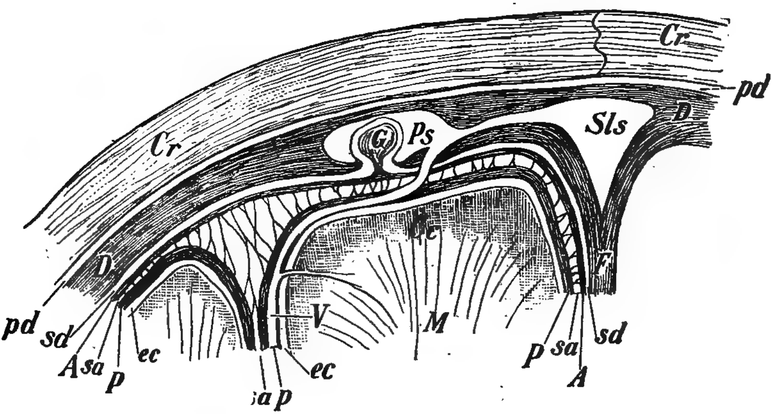



DIAGRAM OF THE CEREBRAL MEMBRANES. (*Obersteiner.*)

*Cr*, cranial bones; *D*, dura; *sd*, subdural space; *A*, *p*, pia arachnoid; *sa*, cellular spaces between its layers; *ec*, epicerebral space; *G*, Pacchionian body; *Ps*, *V*, venous spaces communicating with *Sls*, superior longitudinal sinus; *Cc*, cortex; *F*, falx.

*Suppurative pachymeningitis.* Access of pyogenic germs is facilitated by injury and disease of the cranial bones, and by suppuration in their cavities or the sinuses of the dura. The inflammation may extend from the middle ear, the orbit, or even severe erysipelas of the scalp. The dura is swollen, edematous and altered in color, and extension to the pia is common; less often the lesion begins in the latter and involves the dura. When circumscribed the suppuration may end in scars and adhesions between the membranes. Septic thrombi may form in the sinuses.

Another form of chronic inflammation of the dura leads to fibrous thickening of the membrane in large areas, without pus or hemorrhage, so that it becomes three or four times the normal thickness. The dura is then more adherent to the bone and may contain plates of new bone, as in the falx. Normally the attachment of the dura to the bones is more intimate at the two extremes of life, and at all times over the basis cranii than over the vault.

**Tumors.**—Circumscribed *fibroma,* though not common in the dura, may occupy any part of it, and if large, causes partial absorption of the bone. *Osteophytes* form on the cranial side of the dura, in the falx and tentorium, and along the sinuses. Endothelioma of the dura occurs, and like other tumors of the structure, may contain many corpora amylacea. *Endotheliomata* are either alveolar, or contain long series of endothelial cells in a reticular disposition (fascicular type), or have well-developed vessels with the endothelial cells arranged concentrically about them (plexiform type). They are commonly of moderate size, slow growth, and without metastases. Deposit of mineral salts is common and may constitute psammoma.

*Sarcomata* of the dura may begin as a primary round or spindle celled tumor, or may develop from endothelioma. They are perhaps the commonest dural tumors. They may perforate the bones.

Secondary tumors usually invade the dura from neighboring tissues as occurs with sarcoma of the cranium, and glio-sarcoma of the brain.

*Tuberculosis* occurs with similar disease of the pia (basilar meningitis), or in circumscribed areas with tuberculosis of the bones.

*Syphilis* plays an important part in pachymeningitis, and gumma of the dura may invade the bones or vice versa. Gumma on the inner aspect of the dura involves the pia, and results in firm adhesions.

*Parasites* are uncommon. Cysticercus and echinococcus have been reported.

## THE PIA MATER.

**Disorders of Circulation.**—*Anemia* may occur in general anemia, though often it is not demonstrable after death. *Hyperemia* is common after death in alcoholic and epileptic subjects, in acute rheumatism, with many infectious diseases, poisons (especially alkaloidal), and as the first stage of leptomeningitis. In death during acute mania and delirium of various kinds, and from sunstroke, active hyperemia is commonly found. The general appearance of the membrane is a diffuse red, and even the smallest visible vessels are distended. Under the pia there is usually an excess of serous fluid, which may be blood stained; if inflammation is already begun this fluid is turbid from pus cells. The cortex shares in the congestion. Apparent passive congestion may be only a post-mortem condition; it is especially marked over the posterior aspect of the pia when the body has lain on the back. True stasis occurs in heart and lung disease, thrombosis of the sinuses, and after asphyxia. The sub-pial fluid is increased and the cortex is also congested and moist; on section of the brain the puncta vasculosa are unusually prominent.

*Hemorrhage* occurs in certain infections (anthrax), severe inflammation, and diseases associated with extravasation (scurvy); the blood is usually distributed in small foci over a large area. With injury to the cranial bones, rupture of cerebral vessels, and thrombosis of the sinuses, the bleeding is more massive and may follow the pia from the base over the convexity and into the ventricles. Such layers of clotted blood are commonly seen after rupture of aneurysms at the base of the brain, especially when not immediately fatal. Hemorrhage from the brain into a ventricle may find its way out along the pial insertions and for a greater or less distance under the

external pia. Slight sub-pial hemorrhages in parts distant from important centers may be wholly absorbed and leave only areas of yellow color (ochreous foci) due to the alterations in the blood pigment.

*Edema.*—External hydrocephalus appears in and beneath the pia in general senile atrophy of the brain (hydrops ex vacuo), in stasis, and after death in alcoholic coma ("wet brain"). The pia of the new-born after prolonged labor may be very edematous.

**Inflammation.**—*Acute lepto-meningitis* is described according to the exudate as:

1. *Serous meningitis*: occurs as the first stage of infectious inflammation and also with sunstroke and alcoholism. The appearances in the gross may be those of simple edema, or the fluid may be turbid from pus, but microscopically its inflammatory nature is clearly recognized by the active hyperemia, the infiltration with round cells and pus.

2. *Purulent meningitis*: occurs with similar lesions in cranial bones, disease of the middle ear, the orbit and the nose; also in a hematogenous form, due to the presence of the pneumococcus, by which more than half the cases are caused, or the bacillus of typhoid, of bubonic plague, and the colon bacillus.

The disease may be circumscribed or involve most of the extent of the pia. Masses of pus and fibrin, yellow or greenish, are found over the pia-arachnoid or beneath the cerebral surface, especially marked at times in the sulci of the convexity. Where the process is farthest advanced the pia is thickened and partly hidden by the exudate, and the suppuration may follow the vessels into the cortex and cause abscesses. These lesions may also invade the ventricles and the spinal canal, but commonly the case terminates fatally before such generalization takes place. The distention of the vessels, especially the veins, and the increase in cerebral fluid correspond to the extent of the lesion.

Microscopically the vessels are surrounded by fibrin and pus-cells, the lymph spaces are distended by these elements and swollen endothelia. In the cortex foci of round cells occur along the vessels (both blood and lymph) with degeneration or necrotic changes in the cells and neuroglia. Hemorrhages in the pia are common. Bacilli may be found in numbers or sparingly. The gross appearances are said to correspond to the different organisms, the pus being greenish with b. pyocyaneus, containing yellowish granules in actinomycosis, having a thick yellow look in tuberculous cases, and being more cohesive with pyogenic cocci

3. *Epidemic cerebro-spinal meningitis* resembles the acute suppurative form, but usually begins on the convexity and spreads in all directions to involve the basis. In the fulminant cases death occurs in so short a time that the gross appearances may not resemble inflammation, as in the inflammatory serous edema mentioned above. Hyperemia, punctate hemorrhages, and sub-pial edema are found, and, microscopically, the infiltration with polynuclear leucocytes and the specific organism, the diplococcus intracellularis meningitidis. Associated with the brain lesions petechial hemorrhages in the skin, otitis media, suppuration in joints and endocarditis are observed. The spinal meninges present exactly similar lesions, but the cord is apt to be more severely affected than the cortex of the brain; the posterior surface, in the lumbar region especially, being covered by inflammatory products which follow the posterior nerve sheaths, and at times the central canal is dilated and purulent.

*Chronic inflammation* of the pia is commonly not an independent lesion but follows diseases of the dura and the brain. The process is a chronic increase in connective tissue, which may produce fine projections on the surface (arachnitis villosa) in groups and lines, and thickens the pia over small or large areas. Fatty degeneration and calcareous deposits may occur in the newly formed tissue, and adhesions between the

pia and the dura, or between the pia and the cortex may be very firm. The general effects and symptoms depend upon the location and the thickness of the products. The worst results follow compression and degeneration of cerebral nerves, compression of veins, or obliteration of ventricular openings with resulting hydrocephalus.

*Tubercular Meningitis.* — The exudate is sero-fibrinous or more purulent and in addition tubercles form along the vessels. This process is so frequently developed at the base of the brain that basilar meningitis is a synonym of tubercular meningitis, but it may occur elsewhere. It is commonest in early life but not unknown in adults. While seldom primary such cases may occur; commonly it develops with general miliary tuberculosis or suddenly follows the entrance of tubercle bacilli into the circulation from some chronic process in lymph nodes, lungs or elsewhere.

Frequently the pia in the neighborhood of the pons and the course of the Sylvian artery is first attacked, becoming thicker and slightly opaque, grayish or yellow, and with copious exudate the delicate tubercles may be hard to find by gross inspection. They are minute gray points, usually scattered, and are seen best on the inner surface after careful separation of the pia. At times they are found only after dissecting out a main vessel, as the middle cerebral, with its branches and washing to remove the exudate. In many cases, though most distinct on the basal pia, patient search will discover single tubercles on the pia over the convexity or in the cortex; here they may be grouped and the tissue about them softened. The choroid plexus is a favorite site for their development and the ependyma may show a few. Other places which should be examined are the inner surface of the dura, the membranes of the cord, and the retina.

Microscopically the acute tubercles are made up of endothelial cells, at times polynuclear, but seldom contain giant

cells till the lesion has become chronic. While the relation of the tubercles, single or grouped, to the small arteries and veins is usually clear, other tubercles are found in which such a relation is not evident. If they have existed any length of time degeneration of their centers is common, both hyaline and caseous. Connected with their formation there is marked proliferation of endothelia in lymph spaces, thrombosis of small veins, and copious serous exudate; both round cells and polynuclear leucocytes are found grouped about the vessels and invading the brain substance. Tubercle bacilli are usually easy to find except when suppuration is very marked. The stages of the lesion are thus entrance of tubercle bacilli, endothelial proliferation, and inflammatory reaction, followed by degenerative changes; and both gross and microscopic appearances correspond to the length of the duration of the process. The lesion is hematogenous and secondary in the vast majority of cases, and the clinical symptoms correspond to the reaction rather than the tubercle formation. Especially is this true of the inflammatory edema which has given the disease its other name, "acute hydrocephalus," the ventricles in many cases being much distended by clear or turbid serum.

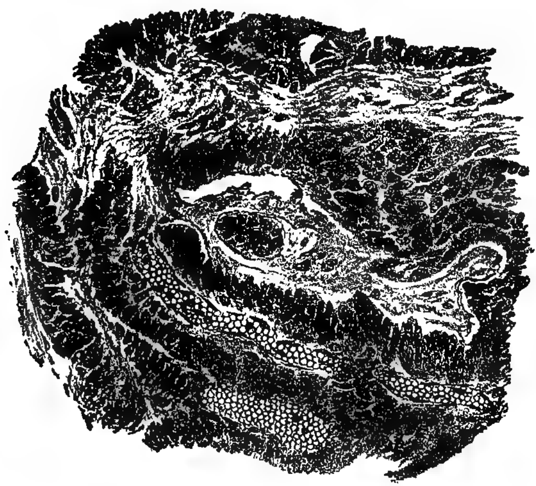
*Syphilis* occurs in the pia as diffuse or limited collections of soft and grayish-red granulation tissue. As the lesion persists the usual caseous softening, absorption, and cicatricial contraction follow. While commonest at the base these lesions may involve any part, and, from the pia, the dura and the brain tissue become affected. In a diffuse chronic form a fibrous hyperplasia, which involves the cortex also, may be found. It is at times difficult to say whether the process has begun in the pia or the dura or the cortex.

**Tumors.**—In nearly every cadaver of adults the Pacchionian bodies are found along the line of the longitudinal sinus on both sides. The cortex, pia, and dura are firmly adherent usually, and the bone is absorbed in a linear series of smooth

depressions, which go nearly or quite through the entire thickness of the bone. These bodies are made of connective tissue, often with calcareous matter, and are without pathological significance.

*Endothelioma* and *perithelioma* develop from the lining or investing cells of the vessels of the pia, either in the choroid plexus or over cerebrum and cerebellum, and, while they sel-

FIG. 120.



ENDOTHELIOMA OF THE PIA. (*Stengel.*)

dom reach a large size, may cause pressure symptoms. They easily undergo colloid changes. A special variety of these growths is known as cholesteatoma, most frequently found in the Sylvian fissure. Lipoma and myxoma have been described, chondroma is extremely rare. Secondary tumors are inevitable with similar neoplasms of dura and cranium.

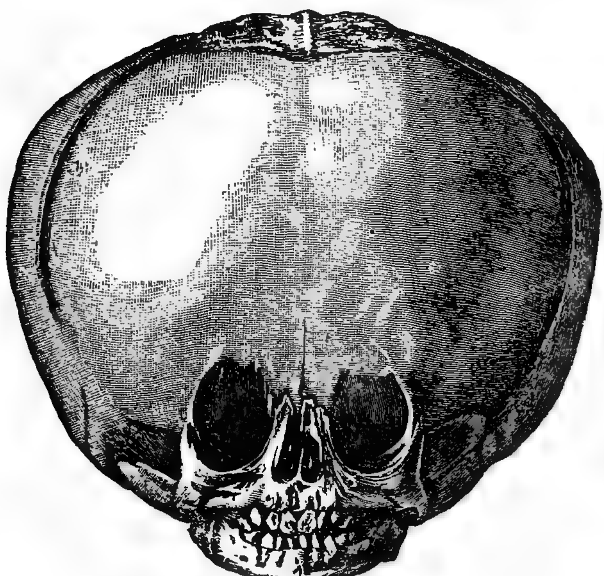
*Parasites* are uncommon. Echinococcus and cysticercus develop at times, in the pial folds of the ventricles or at the base.

## The Ventricles.

**Disorders of Circulation.**—*Anemia* and *hyperemia* of choroid plexus and ependyma are not of pronounced pathological importance.

Massive *hemorrhage* into the cavities occurs with apoplexies which break down their walls, or when after rupture of an-

FIG. 121.



CONGENITAL HYDROCEPHALUS. (*Ziegler.*)

eurysms at the base the blood follows the pia into the ventricles. Large collections by their pressure flatten the convolutions of the side involved. In the new-born the choroid vessels occasionally are torn during instrumental delivery.

*Edema* (internal hydrocephalus) may begin before birth or afterward. Slight congenital degrees may develop after birth

into large collections of serous fluid, flattening the cortex as the ventricles, one or more, become distended, and leading to such internal pressure that the bones of the cranium are separated and the typical hydrocephalic appearances are reached. The head exceeds its proportion to the face by many times, the forehead is prominent, the eyeballs depressed and made prominent, the external auditory meatus distorted, and the fontanelles and lines of junction of the bones increased in extent and closed apparently by thin membrane. Thinning of the bones and abnormal outgrowths (osteophytes) may usually be observed. The dura may be thin or thick, a slight amount of fluid between it and the brain is usual, the cortex is almost without trace of sulci or convolutions, the cerebral tissue is diminished to a thin wall or in places only the pia covers the large collection of ventricular fluid. The lateral ventricles are most dilated and may communicate with each other by destruction of the septum. The ependyma may be thickened and granular. The ganglia at the base are deformed and atrophied. The fluid is usually clear but it may be turbid and contain a large per cent. of albumin. Since the condition steadily becomes more extensively developed the total amount of fluid varies with the stage at which it is examined; it may be only 1--2 hundred grams in the child and a liter or more when the death occurs in later years. The effects clinically are worst when the disease develops acutely with an inflammatory element, and when union of the sutures has begun. In any case the cortex suffers last and least as a rule.

If the accumulation of fluid ceases in early life the patient may live many years, and then the convolutions and the intelligence are more nearly normal. Wormian bones may develop and help to complete the ossification of the skull; as many as twenty of these extra bones have been counted in the sutures of one skull.

The causes of congenital hydrocephalus seem to include heredity in the children of certain women; relatively advanced

age, alcoholic habits and syphilis of the mother; inflammatory processes in the ependyma and choroid plexus; and rhachitis, mechanical obstacles to venous return and chronic cranial inflammations in the acquired form. More definite knowledge is lacking.

**Inflammation.**—*Ependymitis* may be acute or chronic. The former is almost always associated with other acute lesions (meningitis) and characterized by thickening and purulent infiltration of the ependyma and pial folds, or at times softening of the ventricular wall are found and small hemorrhages; the cavity contains serous or purulent exudate. The lateral and the fourth ventricle are the usual seats of the disease. In chronic ependymitis the surface involved is thick and rough, often very granular in small or larger extent, its color is whiter and more opaque than normally, adhesions may form between opposed surfaces or the ventricle may be much distended by serum.

**Tumors.**—Small lipomata and gliomata may occur on the ependyma; angio- and glio-sarcoma sometimes develop on the choroid plexus and the ependyma, and myxomatous degenerations of these. Small cysts in the plexuses are very common.

Cystic *parasites* have been found in the ventricles, lying free or attached.

## The Brain.

**Malformations.**—Unusually small brains (microcephalous, hypoplastic) occur with premature union of the bones and independently; the condition may coexist with moderate hydrocephalus. Complete defect (anencephaly) is observed in non-viable infants, in the highest degree with defect of the posterior aspect of spine and cranium; more or less completely developed nerves may be found even in these cases. Less extensive faults of posterior closure with hernia of the cranial contents have been mentioned in Part I., p. 28. The contrary

condition, macrencephaly, is rare, and results from increase in the connective tissue in the brain.

**Disorders of Circulation.**—*Anemia* of the brain is characterized by paleness of both cortex and white substance, absence of the puncta vasculosa on section, and increased firmness of the organ; the ventricular fluid may be increased. General anemia, extensive hemorrhage, arterio-sclerosis of the cranial vessels, intracranial pressure, cachexia, and vaso-motor constriction are the chief factors in its production.

*Hyperemia* is active in cases of sunstroke, delirium and local inflammation, in mania and some infectious diseases. If well developed the membranes appear under tension, their vessels are prominent and distended, their color is red and the same is true of the cortex, the puncta vasculosa are numerous and large. Microscopic search may discover small capillary extravasations, or at least a diapedesis into the peri-vascular lymph spaces. In passive congestion the causes are the usual impediments to venous return and the color of the parts is bluish rather than red. Congestion may be general or affect only certain areas, and after death there may be no marked increase in the cerebral blood when there has been reason during life to expect intense congestion.

*Edema* of the brain may leave no clear evidences post mortem, with the same symptoms in one case there may be no edema, and in another it may be unmistakable; on the contrary, well-developed edema of the brain has appeared in some cases to be a terminal or even a post-mortem phenomenon. Hence if present, its interpretation requires careful consideration of all the factors of the case. A moderate degree of edema is common in aged subjects and is supposed to be compensatory for the cerebral atrophy. Other slight edema appears as increased sub-arachnoid and ventricular fluid; with venous stasis in addition the brain itself is infiltrated, its tissue very soft and usually post-mortem changes are rapid. On gentle pressure a few drops of clear fluid may be expressed from perivascular

lymph spaces. In children especially, sudden development of cerebral compression symptoms (as in basilar meningitis) appears to correspond with rapid edema of the brain, which is then found moist, its convolutions flattened, and the ventricular fluid increased. In alcoholic cases well marked edema is so common that "wet brain" and "serous apoplexy" are sometimes returned as entirely satisfactory explanations of the manner of death. The contrary condition, remarkable dryness of the brain, occurs in cholera and other infectious diseases, both with and without large bodily discharges (sweat, urine and feces).

*Hemorrhage.*—Massive bleeding into the substance of the brain may follow severe blows on the head, with fracture of the bones as well as independently, and the hemorrhage may be directly under the application of the force or on the opposite side. Thus a blow received on the occiput may be followed by bleeding on the tips of the temporal and frontal lobes, or if on one parietal boss may cause bleeding along the opposite Sylvian fissure.

Two explanations are offered for these conditions. The first supposes that waves of force are propagated in all directions from the point of violence, but at different rates and intensities, by the two tables of the skull and varying thicknesses of bone, so that where they meet, at a point more or less opposite the point of impact, by their jarring they disorganize the brain substance and tear the vessels. The second is based upon the elasticity of the cranial bones, and assumes a temporary depression at the point of injury and a rapid and sudden bowing out of the sides and depression at the opposite side; and when this distant depression, which compresses the brain, is released, a hiatus occurs which the soft brain tries to fill out, and the strain bursts, or explodes, the vessels. Neither theory is wholly satisfactory.

Apart from traumatism, bleeding from cranial vessels is

known as *apoplexy*, and is of two varieties, according to the size of the clot. The small, and often numerous, foci are called capillary or punctate hemorrhages, while the large, and usually

FIG. 122.


APOPLECTIC CLOT IN THE SUBSTANCE OF THE LEFT HEMISPHERE. (*Ribbert.*)

*F*, sylvian fissure; *V*, lateral ventricle; *L*, lenticular nucleus. The clot invades the surrounding brain by irregular projections, and has broken into the lateral ventricle.

single clots are termed apoplexy. Two factors concur in their formation, weakening of the walls of the vessels and increase of the intra-vascular pressure. The affection of the vessel wall

may be part of a general arterial disease, as in senile atheroma; or a sudden decrease in resistance in severe infectious disease (anthrax); or a local dilatation may reach a certain grade and remain for long periods, only to rupture on sudden muscular and emotional excitement, as is observed with aneurysm of cerebral arteries.

Increased blood pressure with hypertrophy of the left ventricle will not rupture the vessels of the brain, but the arterial degeneration is so commonly associated with cardiac enlargement that it is usual to find both in apoplectic cases. The aneurysm may be single and large, or multiple and miliary, requiring careful search; the latter form is often observed in the optic thalamus, caudate and lenticular nuclei, pons and medulla.

Not every cerebral apoplexy is associated with aneurysm of the local arteries. Quite frequently apoplexy occurs in young and vigorous subjects, in whom a well-marked hypoplasia of the aorta suggests developmental anomalies of the entire vascular system, probably defect of the elastic fibers of the media. The external genitals and the lower half of the body are often noticeably ill-developed.

Capillary rhexis may occur in encephalitis, extreme active hyperemia, embolism and various hemorrhagic states. The blood is limited to the perivascular lymph space or invades the adjacent brain substance, and is followed by red or yellow softening, cystic changes, or fibrous scars. Any part of the brain may present such lesions but perhaps they are commonest in the cortex, where their importance is relatively less serious than elsewhere.

Apoplexy may result from single large bleedings or the rupture of numerous capillaries. As the blood is forced out of the vessel the brain tissue is softened and destroyed, the resulting clot usually lying in the middle and having finer subdivisions which pierce the tissue in all directions. If near a cavity this

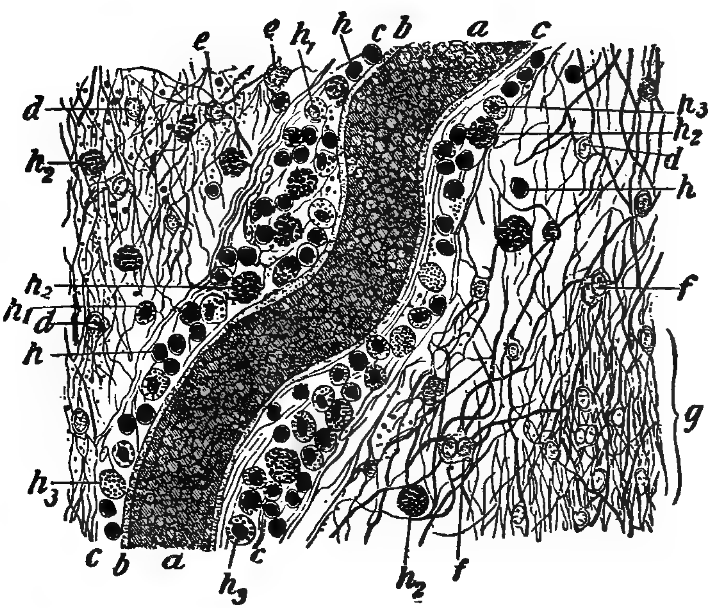
destruction usually involves its wall, and thus the entire ventricular system, or any part of it, may be filled with clots which more or less completely reproduce the form of the cavity. In these cases the cortex is apt to be much flattened and perhaps anemic from the combined loss of blood and pressure.

The clinical results of apoplexy depend upon the extent and the localization of the hemorrhage. If the patient survives, the blood may be absorbed and leave only crystals of hematoidin and thickened neuroglia at the site, or it may become encapsuled (rarely by a distinct fibrous membrane) and undergo softening with loss of pigment, forming an apoplectic cyst. If under the pia, this membrane becomes thick and opaque, the blood is entirely absorbed, and the surface consequently depressed. In point of frequency the corpus striatum is most commonly the seat of apoplexy, and the artery involved is the lenticulo-striate, which from the mechanical conditions is peculiarly liable to nutritive lesions. The thalamus, the hemisphere (extra-ganglionic), the cerebellum, pons and medulla are less often involved.

*Thrombosis and Embolism.*—Disease of the vessel wall, in medium- and small-sized vessels, narrows the lumen, and by slowing the circulation beyond favors the formation of thrombi. A portion of such a thrombus may be loosened from the wall and carried farther till it occludes the vessel, or emboli from the left side of the heart may lodge in some of the cerebral vessels, most commonly in branches of the middle cerebral. The results correspond to the loss of function in the part supplied, which soon begins to degenerate. *Red infarction* seldom occurs, owing to the anatomical relations of the veins, their entrance into the large sinuses of the dura being accompanied by great decrease of pressure within them. If the flow of blood in the sinuses is much impeded, by thrombosis or other cause, red infarction may develop and most often in the cortex and immediately adjacent white substance.

With embolism, and coagulation about the embolus, nutrition in parts beyond suffers immediately, and softening of the part is rapid; in obliterating arteritis the degenerative results are more gradual. This softening (encephalo-malacia) begins

FIG. 123.




DEGENERATION IN THE BRAIN. (*Ziegler.*)

*a*, small artery; *b*, its walls; *c*, peri-arterial lymph space, crowded with cells; *d*, *e*, *f*, glia cells with one or more nuclei; *g*, glia tissue, edematous about the vessel; $h$-$h_3$, red cells and leucocytes, some of the latter are loaded with pigment and detritus.

with edema of the part and consequent swelling. Hemorrhage gives the area a red color, its partial transformation and absorption makes it yellow; without this added element the color is white or grayish. In the latter case the tissue is so fluid

that it escapes on section of the part, leaving an irregular cavity with soft, necrotic walls, not sharply circumscribed from the healthy brain. The nerve fibers are swollen and in fragments, there are many granular bodies; a few or many swollen and degenerated ganglia may be found if the cortex is included. The vessels are either collapsed or filled with granular detritus, and droplets of myelin and compound granular bodies are found. Absorption of the resulting milky fluid may follow if a fatal termination is postponed, and then clear serum may take the place of the disorganized tissue. Red softening is practically the same process of liquefaction in an area mixed with extravasated blood, but owing to the presence of clot the fluid is seldom so thin as in the gray necrosis. As the blood pigment undergoes its customary changes the color becomes less bright and takes on a browner hue. Fatty degeneration and an inflammatory reaction are common. The later stages of the process give rise to the yellow softening, or, with but little admixture of red cells, the area may be yellow from the first. Both the red and the yellow foci may be transformed into cyst-like cavities, or encapsuled by hyperplasia of the neuroglia, or contracted into more or less pigmented scars.

**Inflammation.**—A certain degree of inflammatory reaction in the cerebral tissue is commonly observed about hemorrhages, tumors, and foci of softening, but in many cases the inflammation concerns the vessels and the brain suffers more strictly degenerative changes. Inflammation apart from these forms may take its origin in the vessels or the connective tissue of the organ, and here also the various elements suffer passively for the most part. In its course it may be acute or chronic, in its nature it is exudative or productive, and its distribution may be diffuse or circumscribed.

The causes of encephalitis are in many cases difficult to determine. In others traumatism of various kinds, foreign bodies, sunstroke, alcoholism, access of pyogenic organisms, and the presence of infectious disease in other organs explain the at-

tack; at times more than one of these conditions exists. In some cases the brain appears to have increased in both size and consistency, due to inflammatory serous infiltration. The gross appearances may not suggest inflammation. On microscopic examination the exudate is found chiefly in the perivascular lymph spaces, accompanied by red blood cells. In chronic cases the neuroglia appears to have increased in quantity and ganglia and nerve fibers show degenerative changes. The name sclerosis is sometimes applied to this condition.

*Hemorrhagic encephalitis* is an acute inflammatory process involving the cortex, which has been observed in connection with infectious diseases, as influenza, diphtheria, scarlatina, and erysipelas. The vessels are acutely hyperemic and in the tissue about there is diapedesis of red cells and infiltration with leucocytes. The axis cylinders are tortuous and in many cases there is a degeneration of the ganglion cells and processes. In a later stage many large epithelioid cells are found, but these occur in other lesions, as softening.

The course of the disease is usually acute and fatal, but recovery may be complete or there may be paralyses and loss of special senses.

*Abscess* of the brain is frequently secondary to disease of the middle ear, injury to the cranial bones and membranes, suppuration in the nasal cavities, and septic embolism (pyemic). In other cases no cause can be assigned (cryptogenic). The course of the disease is often very slow, the abscesses may be single or multiple, and even large ones may be discovered only at autopsy, having given no striking symptoms. According to the stage in which this form of encephalitis is examined, a focus of what looks like yellow softening, perhaps hemorrhagic also, or a well-developed abscess cavity may be found. In the latter the pus is either yellow or green, and fluid, or thickened and caseous, surrounded by attempts at capsule formation. Rupture into the ventricles may occur, and escape of the pus outward has been observed, through the middle and external

ear when the bone has been perforated, through the ethmoid and the nasal cavity, and elsewhere.

*Cerebral Sclerosis.* — Chronic hyperplasia of the neuroglia may be diffuse or local. Disseminated sclerosis occurs in alcoholic subjects and in late stages of dementia paralytica. The organ is pale, firm and elastic, its total volume may be lessened, the convolutions are slender (microgyria), and hyperplastic changes with pigmentation are noticeable about the vessels, which may be very tortuous. The nerve cells and ganglion cells may show degenerative lesions. Localized sclerosis (in placques) sometimes involves a single convolution or part of one, or numerous hardened places occur in both brain and cord. They are firm, often sharply defined, and vary in color from gray, reddish gray and white to yellow; on section they may project above the general surface or be depressed. Other areas in the same brain may be softened. Fatty granular cells, fragments of nerve fiber, hyperplasia of the connective tissue, thickening of the vessel walls, and corpora amylacea are found in these areas; and corresponding to the fatty degeneration of ganglion cells (in the cortex) the lymph spaces contain granular fatty material.

*Dementia paralytica.*—A peculiar cortical lesion which develops between the ages of thirty and fifty, in men more than women, and associated with gradual loss of memory, is called dementia paralytica. Syphilis, alcohol, mental fatigue and injuries to the head are the commonest causes. In children rare cases are observed with congenital syphilis.

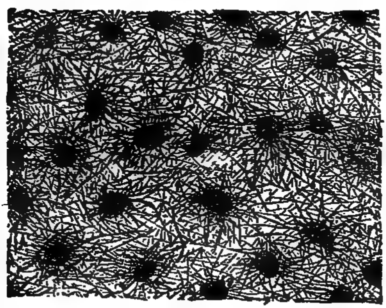
The dementia develops slowly, there are tremors of the tongue, lips and extremities, characteristic disorders of speech, Argyll-Roberston pupils, and at times apoplectic attacks.

The cortex is atrophied, especially in the frontal and parietal regions. Over such areas the pia is thick and adherent. In the ventricles the ependyma may be the seat of inflammatory changes, and, with this, internal hydrocephalus may follow. The total weight of the brain may be only 900 gm.

Microscopically the vessels show thickening and hyalin degeneration, with dilatation of the lymph spaces. The glia tissue is increased and the nerve cells are degenerated or decreased in number. Small nerve fibers, especially of the tangential layer, are also fewer in number. Similar lesions may be found in the thalamus and the spinal cord.

**Tumors.**—*Glioma*—Three forms of this neoplasm have been described, the simple hyperplasia of the neuroglia to which the name glioma was first given; the neuroglioma which includes,

FIG. 124.



SECTION OF A GLIOMA. (*Ziegler.*)

as the former excludes, participation of nerve cells and fibers in the neoplasm; and the rare "neuroglioma ganglionare," or cerebroma, in which hyperplasia of ganglion cells is said to occur. The tumor is commonly spherical, not sharply defined against the brain tissue, and varies in consistence between soft and myxomatous forms and firm, denser growths. If the blood supply is free hemorrhages are usual in the tumor, and a certain degree of reactive inflammation about it may be present. In the very soft forms a cystic transformation may develop. The commonest sites of such tumors are the interior of cerebrum and cerebellum, the pons and the medulla, but they may develop in any part of either brain or cord.

The microscopic appearances include hyperplasia of the neuroglia with round and flattened cells in its meshes, or relatively numerous cells with short processes in feebly developed fibrous tissue, with newly formed vessels, and small or massive hemorrhages and granules of mineral matter. The course of these tumors is rather slow, their size is seldom large and they do not invade other tissues or form metastases.

*Sarcoma* of the brain may develop from the membranes and invade the cerebral tissue, or begin in a glioma or as a primary tumor. Angio- and myxo-sarcomas occur, as also spindle celled and endothelial forms. All forms of sarcoma grow rapidly, invade other tissues and even perforate the cranial bones. As secondary tumors both sarcoma and carcinoma occur in the brain, either by direct ingrowth from the exterior or by embolism in extensive disease of malignant nature.

*Tuberculosis.*—With tubercular meningitis it is commonly the case that miliary nodules may be found in the brain also. Solitary tubercles sometimes develop, independently of disease of the membranes, in any part of the brain. The centers of such tubercular regions are apt to be dry and caseous, the edges gray and translucent; in the latter the characteristic miliary tubercles are found. The largest of these foci are often plainly made up of conglomerated solitary tubercles. Their situation is usually basal, and they occur most often in children with tubercular disease of the lymph nodes and other organs.

*Syphilitic gumma* commonly begins in the pia and invades the brain, or in the dura, forming adhesions between itself, the pia and the cortex and then attacking the latter. The center of the mass is commonly yellow and caseous, the periphery grayish or reddish and translucent; in old cases the customary absorption and shrinking are observed.

In other cases of syphilis the brain is affected secondarily, in the form of areas of softening, or sclerosis, due to marked endarteritis.

*Parasites.*—Various bacterial forms occur in the brain; *e. g.*, the diplococcus pneumoniæ is the most frequent cause of acute suppurative meningitis. Actinomycosis invades the organ secondarily. Echinococcus and cysticercus are rare but have been found; of the two the latter is the more common.

## The Spinal Membranes.—The Dura.

*Hemorrhage.*—Extravasation of blood may be found in the epidural tissue, where it is usually confined to small areas, or in the subdural space, where it may spread the whole length of the cord. The causes are injury, from force externally applied, and great intravascular pressure, developing in tetanus, trismus neonatorum and strychnine convulsions.

When the blood is limited to the epidural tissue it may cause slight pressure on the nerve roots, or even upon the cord. When larger hemorrhages take place into the subdural space there are symptoms of irritation, pain along the cord, stiffness of the spine, hyperesthesia, muscular spasms, and loss of motion and sensation. A mild inflammatory reaction may follow, and after a time the blood is absorbed.

**Inflammation.**—*Acute pachymeningitis* may be primary or follow disease and injury of the vertebræ. The exudate may consist of fibrin, serum or pus, but is usually purulent and the pus may be copious. The posterior aspect of the cord usually presents the largest amount, owing to the position of the patient before death and of the cadaver afterward. The pus may be found on both sides of the dura, next to the bone as well as next to the pia. When confined to the outer aspect the disease is termed peripachymeningitis, and when the internal face of the dura alone is purulent it is called internal spinal pachymeningitis.

*Chronic hemorrhagic spinal meningitis* resembles the similar lesion of the brain, and occurs in chronic alcoholic patients and with some forms of insanity. On the inner aspect of the

dura there is more or less diffuse membrane made up of new connective tissue and extravasated blood.

Chronic pachymeningitis may follow an acute attack, or be of chronic type from the beginning. This is the case with the hypertrophic form of the cervical region, which commonly begins in the lower cervical area, involving the median and ulnar nerves, and proceeds both upward and downward. It may also begin elsewhere. The cause may be injury, exposure to cold, and syphilis.

The membrane becomes thickened to as much as 2 cm., and is found to consist of several layers of tough fibrous tissue, with adhesions to the pia and the bone. The lesion may involve the roots of the nerves by pressure or by directly invading them, with resulting degeneration. Since the cord becomes affected, by extension of inflammation, both ascending and descending degenerations are observed.

*Tubercles* occur with caries of the vertebræ or with similar disease of the pia, and the caseous masses may exert pressure upon the cord or the nerve roots.

*Syphilitic gumma* and pachymeningitis are less common in the spine than in the brain.

**Tumors.**—Bony plates may form in the dura, fatty hyperplasia between it and the bones is not uncommon, especially posteriorly, and circumscribed lipoma and fibroma and various secondary invasions have been described.

## The Pia Mater.

*Hyperemia* of the membrane occurs actively with various inflammations, and passively in atrophic and cicatricial conditions of the cord.

*Hemorrhage* occurs in scurvy and purpura with hemorrhagic cases of the exanthemata, in asphyxia of the new-born, after injury, and as a diapedesis in extreme hyperemia. Large

masses of blood may have been forced into the spinal canal from cerebral apoplexy and rupture of aneurysms at the base, and be found as partly decolorized clots, but a true spinal apoplexy also occurs.

**Inflammation.**—Purulent spinal leptomeningitis may involve the pia and the inner aspect of the dura at the same time, and extend the entire length of the cord with the exception of the medulla and the upper cervical region, or involve these regions also. The causes are the same as for the cerebral lesion. The exudate, with varying proportions of serum, fibrin and pus, is found in the fissures of the cord, about the nerve sheaths, and generally over the cord; it may invade the cranial cavity from the spinal. Frequently it appears to have started in a limited area and to have spread either upward or downward. Meningo-myelitis implies inflammation of both cord and membranes.

In the gross the cerebro-spinal fluid is turbid and milky, or yellow with pus, and in the former case flocculi of fibrin may be suspended in it. The pia is edematous, swollen, opaque, and perhaps hemorrhagic. The nervous tissue is hyperemic to varying degrees and may be soft and edematous.

Microscopically the intensely hyperemic vessels and the purulent infiltration are very apparent, and along the septa of the cord there is a round celled invasion of the nervous tissue. True abscess formation is not so common as in the brain. The nerve roots may be the seat of purulent invasion, and the formation of exudate may lead to neuritis and degeneration of the fibers.

Leptomeningitis follows caries and injuries of the spine, empyema, and various infectious diseases. It also occurs in an epidemic form as *cerebro-spinal meningitis,* and here the cause is the pneumococcus, or the meningococcus, and other cases are due to a streptococcus. The organism is found during life, after puncture and removal of some of the spinal fluid, in the bodies of the pus cells.

*Tuberculosis* affects the upper portion of the pia in the cervical region with similar disease of the cerebral pia. It occurs in other cases near tuberculous caries of the vertebræ.

**Tumors** of both benign and malignant forms may be found in the pia, primary in this membrane or invading it from the dura. Owing to the rigid walls of the canal and the small space for enlargement, tumors rapidly cause pressure on the cord, with degeneration, or even erode the bones.

## The Spinal Cord.

**Disorders of Circulation.**—*Hyperemia* of the cord, like *anemia,* is often difficult to determine after death. When active hyperemia persists the cord is of a brighter red than normally, and when this is accompanied by punctate hemorrhages it is evident that there has been intense hyperemia before death. Passive hyperemia presents the usual tortuous and distended veins and a bluish tinge in the parts, but a certain degree of this is merely hypostatic.

*Hemorrhage* in the substance of the cord is less common than in the brain. It may be either one or more minute points or larger masses of bleeding. The former variety occurs in death with convulsions (tetanus), with softening and about tumors, and sometimes after extreme congestion. The blood may bore its way along the nerve fibers or rupture into either the spinal or the central canal. The blood goes through the same changes as elsewhere.

Several varieties of spinal hemorrhages are recognized: (1). Accessory hemorrhage, consisting of miliary points about capillaries, causing no laceration nor pressure. Observed with inflammation, softening, and infections.

(2). Traumatic hemorrhage. The amount depends upon the severity of the laceration of tissue. When fracture of a vertebra causes laceration of the cord the symptoms of the latter mask any symptoms which the hemorrhage would cause. But

in some cases of concussion of the cord, without laceration, hemorrhage occurs which produces marked symptoms. The blood is found in the gray matter usually, extending up or down in either the anterior or the posterior horns, or both.

(3). Spontaneous hemorrhage is less common than in the brain, because in the latter the arteries are more generally terminal and the blood pressure is higher. The causes are the same for both, including injury, muscular exertion, cessation of menstruation, and hemorrhagic diatheses.

(4). Hemorrhage in tissue altered pathologically. These cases include softening, myelitis and tumors, but it is not always easy, without clinical observation, to determine which was the antecedent lesion.

(5). Hemorrhage from altered barometric pressure. This form is nearly confined to workers under increased pressure, as divers and those employed in caissons, and the lesion develops on passing from the greater pressure to the normal. The symptom of most importance is paralysis, and the usual lesion is hemorrhage in the cord or brain. It is supposed, in part upon the findings in experimental studies, that emboli of gas form in the blood and deprive portions of the nervous tissue of nutrition, and that the hemorrhage occurs in such regions after softening.

After any hemorrhage in the spine the clot and the lacerated tissue act as irritants, and hence there is an inflammatory reaction. Regeneration does not occur, and hence the best outcome of the lesion is healing by fibrous repair, but this involves some loss of function, usually, and more as the cicatricial tissue contracts. The histological changes are as follows:

The nerve cells show tigrolysis and their nuclei become eccentric. Both nucleus and nucleolus may lose their affinity for certain stains and become fragmented, and vacuoles form in the cell body, and at last the cell is wholly disorganized, converted into a granular detritus which the phagocytes englobe and remove.

The fibers present swelling of the myelin, tortuous and varicose axis cylinders, and fatty degeneration. Extravasated blood gives the part a red color, which varies toward yellow as absorption goes on. Hematoidin crystals and granular pigment may remain for a time. Other elements are large epithelioid cells and leucocytes, both poly- and mononuclear.

When fibrous repair does not occur the broken-down tissue is replaced by serum and a cyst forms, but this is less common than in the brain.

*Crushing of the cord,* with or without laceration of the membranes, is followed by changes similar to those observed after hemorrhages. Usually the cause is fracture, or dislocation of a vertebra. When the injury is followed by infection purulent myelitis and meningitis may result. A slight degree of inflammation occurs in any case, but in the absence of infection is confined to the site of injury and may subside. Secondary degeneration commonly follows.

Edema of the cord develops about inflamed portions and tumors, and causes swelling and succulence of the tissue.

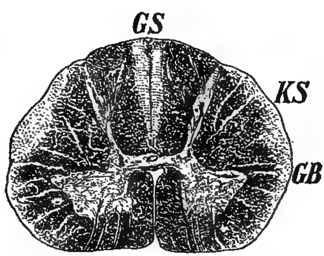
*Thrombosis* and *embolism* are most important when the medulla is involved. Embolism is more common in the left vertebral than in the right. Thrombosis occurs with inflammation of the arterial walls. Both conditions are rare. The immediate result may be sudden death, or anemia and softening, with perhaps a hemorrhage later into the softened focus. The fate of the tissue is the same as in similar cerebral lesions. In the rest of the cord multiple embolism and areas of softening may be found.

**Degeneration.**—The essential element in many of the lesions of the central nervous organs is the complete destruction of their functional constituents. The ganglion cells disappear, after certain changes, the myelin sheaths become broken up into granular and fatty detritus, and the axis cylinders become atrophic and are lost. The destroyed tissue is removed, either by solution in the lymph stream or by being taken up by

phagocytes, which are leucocytes at first and later large endothelia derived from the lymph structures.

All these changes are grouped under the head of degeneration and are usually inflammatory in their nature. The blood vessels and the glia may resist the process or also degenerate and be removed, but the glia usually proliferates, under the irritation of the dead tissue, and causes a fibrous repair. Such fibrous hyperplasia is termed sclerosis, and late contractions produce deformity of the nervous tissue and further loss of function in many cases. The fibrous tissue may also develop from the endothelia of blood and lymph vessels.

FIG. 125.




ASCENDING DEGENERATION IN THE CERVICAL CORD. (*Obersteiner.*)
*GS*, the columns of Goll; *KS*, the lateral cerebellar tract; and GB, Gower's tract, are involved.

Owing to the peculiar relation of the nerves to their neurons, when pathological changes affect the latter, or the axis cylinder becomes separated from it, the nerve undergoes a total degeneration. The converse of this is true, to a less evident degree, for lesions of the nerves may result in atrophy of the ganglia.

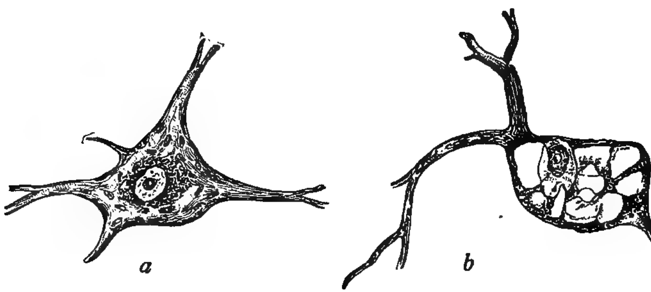
Hence the usual result of a lesion in the brain or the cord is a progressive lesion along certain nerve fibers, and such degeneration is described as ascending or descending when it occurs in the cord. The former occurs in the posterior col-

umns ,which contain sensory fibers progressing upward to the brain, and the latter in the lateral and anterior portions of the cord, containing the motor tracts.

Secondary ascending degeneration results from destruction of ganglion cells in the cord and follows the columns of Goll and Burdach and the cerebellar tract. Just above the lesion the degenerated fibers are proportionately numerous. Higher up the entrance of new fibers lessens their number.

Below a spinal lesion the lateral pyramidal tracts, the crossed pyramidal tracts, and other motor bundles exhibit the descending degeneration. If the lesion is above the decussation, the

FIG. 126.




CELLS FROM THE ANTERIOR HORN IN MYELITIS. (*Obersteiner.*)
*a*, granular degeneration; *b*, vacuoles.

lateral tract of the same side and the crossed tract of the opposite side are involved. When the lesion is below the decussation but half of the cord, or part of it, is affected by descending degenerations on the same side. Complete transverse lesions involve both sides, but sometimes unequally.

Primary degenerations may involve the motor tracts chiefly, as in amyotrophic lateral sclerosis and progressive muscular atrophy; or the sensory tracts, as in locomotor ataxia; or both varieties, as in ataxic paraplegia. Such affections of principle groups of fibers are called systemic diseases.

**Inflammation.**—*Myelitis*—Clinically the term myelitis includes all diseases of the cord which cause symptoms of a diffuse lesion, involving motor and sensory, trophic and reflex systems. It is not always possible to say before death whether the lesion is a liquefaction necrosis of part of the cord, following occlusion of a vessel, or a true inflammation, or a combination of these, perhaps with an element of hemorrhage added.

The etiology of myelitis includes infection as one of the most important causes, and this may be hematogenous, as in variola, typhoid, malignant endocarditis, tuberculosis, etc.; or it may be lymphogenous, as in ascending infectious neuritis with secondary myelitis, gonorrheal cystitis, and purulent conditions about the vertebræ and pelvic bones. Poisons, like carbon monoxide and certain metals, and the toxins of hydrophobia, tetanus, and diphtheria, also cause softening which may resemble myelitis from a diffuse lesion.

The following histological types are distinguished:

(1). Parenchymatous degeneration. In this the fibers and cells are chiefly affected. The whole fiber is swollen to two or three times its normal size, and does not stain well with hematoxylin, and the axis cylinder is tortuous or irregularly thickened. In the myelin are small fatty globules, which increase until the whole substance is degenerated. Edema may be prominent throughout the tissue involved. There are but few leucocytes, and no epithelioid cells until late stages.

(2). Infiltration. Here the characteristic element is the profuse invasion of the tissue by polynuclear leucocytes and a few mononuclear cells. They appear about the blood vessels, in the perivascular and other lymph spaces, and afterward spread through the tissue along the fibers and the lymph spaces about the nerve cells. The process either destroys the tissue or ends as a chronic productive inflammation. The vascular changes are most prominent in this type.

(3). Softening; myelomalacia. Since there are fewer large terminal arteries in the cord than in the brain, and since the spinal vessels do not suffer sclerotic and degenerative changes so frequently, myelomalacia is not so common as the similar cerebral lesion. The softening is caused by some vascular lesion, thrombosis, embolism or obliterating endarteritis, and this produces liquefaction necrosis. Hence in this third type, which strongly resembles myelomalacia, the characteristic element is the presence of large epithelioid cells which are phagocytic derivatives of the endothelia of lymph and blood vessels. They take up large amounts of fatty detritus and remove it. In the early stages the vessels show an invasion of leucocytes in their walls and surrounding lymph spaces. Hemorrhages may occur with either of these types.

When myelitis occurs diffusely through the cord it is called disseminated; when it is confined to one segment, it is called transverse. Leucomyelitis implies that the white substance is especially affected, and poliomyelitis that the gray matter is alone involved.

*Acute anterior poliomyelitis.* The lesion may be diffuse or transverse, but in any case is confined to the anterior horns, and hence might be classed among the systemic diseases, although it is an acute inflammation. Owing to its appearance chiefly in children, before the fourth year, the disease is called also spinal infantile paralysis. At times it occurs in the adult.

The initial stages are those of an infection, though in some cases there is no fever. After a few days a group of muscles in one leg may be paralyzed, and the paralysis, after extending along the limb as well as to other limbs, may either disappear entirely or leave certain groups of muscles affected. In the severe cases the paralysis is flaccid, the muscles atrophy and have the reaction of degeneration.

The lesion in the anterior horns is explained by two hypotheses. According to one the virus especially affects the nerve cells, producing degeneration of them, hyperplasia of

the connective tissue and alterations in and about the blood vessels. The other explanation assumes an acute inflammation of the tissue in the anterior horns which causes degeneration of the ganglion cells secondarily. In some cases there is pro-

FIG. 127.

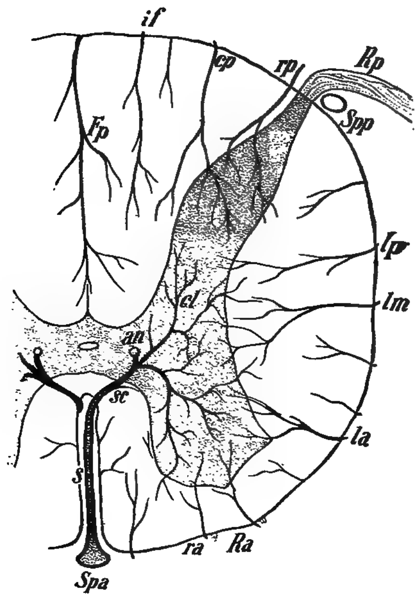



DIAGRAM OF THE ARTERIES OF THE CORD. (*Obersteiner.*)

*Spa*, anterior spinal; *s*, artery of the sulcus; *sc*, sulco-commissural branch, and *an*, its anastomotic branch. *Ra*, anterior nerve root, and *ra*, its vessel. *la*, *lm*, *lp*, lateral arteries, anterior, middle and posterior. *Spp*, posterior spinal art. *Rp*, posterior nerve root, and *rp*, its vessel. *cp*, art. of the posterior horn. *if*, interfunicular branch. *Fp*, art. of the posterior fissure.

fuse infiltration of leucocytes, and in others this is absent; possibly there is positive cytotaxis in the one case and negative in the other.

The vascular supply of the cord is important in determining the lesion in the anterior horns. There are two systems of vessels, the ventral and the dorsal.

In the ventral system a branch passes down from each vertebral artery and these unite to form the anterior spinal artery, which lies in the ventral sulcus. From this, small branches pass into the sulcus, the sulco-commissural arteries, and then pass into the gray matter of the anterior horn, send a small branch to Clarke's column, and supply a narrow margin of white matter about the anterior horn. A small branch passes up and another one down in the gray matter, anastomosing with others above and below. At the bottom of the sulcus these arteries do not divide, by sending a branch to either side, but the entire artery turns either to the right or the left anterior horn, alternately. These arteries supply certain segments on either side and also special groups of cells. This arrangement accounts for the localization of the lesion in certain segments or special groups of cells, for the toxic agent affects only the region supplied by one or more of these main arteries.

In the dorsal system small branches from the vertebrals unite with others from the intercostals, and pass around the cord in the pia, supplying the white matter and the posterior horns. In anterior poliomyelitis and Landry's paralysis the ventral system is involved, while in acute and chronic leucomyelitis the dorsal vessels, or system of the vaso-corona, are more affected.

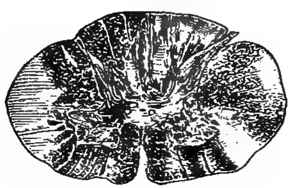
**Acute Ascending Paralysis**, or Landry's, may occur at any age. While some cases present prodromal symptoms, others develop quickly. Paralysis begins in one leg and extends to the other, or in both at the same time. It then involves the muscles of the thighs and trunk, and ends fatally when the muscles of respiration and deglutition are attacked. While the main symptoms are motor, sensory disturbances often accompany them, as hyperesthesia or paresthesia, with diminution

of the cutaneous and deep muscular senses. The bladder and the rectum are not affected.

The paralysis is flaccid, but there are usually no atrophies. The reflexes from the skin may be diminished, while the tendon reflexes remain normal or are also lessened. In rare cases the paralysis is descending instead of ascending. Recovery is possible.

The lesions may be found in the nerves, gray matter and medulla. In some cases there is an acute inflammatory lesion, with serous exudation, and cellular infiltration about the vessels and in the lymph spaces. In other cases there is no inflammation, but tigrolysis, eccentric position of the nucleus, irregularities in the nucleolus, and vacuoles in the cell body are found.

FIG. 128.



DISSEMINATED SCLEROSIS IN THE CERVICAL ENLARGEMENT. (*Obersteiner.*)

**Multiple Sclerosis.**—This might be classed with myelitis, for it involves the brain and cord irregularly and diffusely. The sclerosed areas may be only about the size of a pin's head or several cm. in diameter.

The disease may follow acute exanthemata, chronic metallic poisoning, and injury, but the etiology is obscure. It usually develops between the tenth and the thirtieth year.

The main symptoms are intention tremor, scandinating speech, nystagmus, spastic condition of the limbs, and exaggerated tendon reflexes.

In the gross the lesions resemble the normal gray matter; after hardening in bichromate of potash solution they are much lighter than the surrounding white or gray matter. The diseased tissue may be sharply circumscribed or fade into normal tissue gradually. The light color is due to the absence of myelin substance. The axis cylinders persist for a time and retain some power of transmitting impulses.

In one type of the disease vacuoles are common throughout the diseased tissue, with epithelioid cells, and corpora amylacea. The glia does not proliferate freely and hence does not fill out defects left by the vanishing myelin substance. In the other type there are no vacuoles, and few epithelioid cells, but the glia is markedly hyperplastic. There is more or less complete stasis of the lymph and hence the lymph spaces appear distended.

**Syringomyelia.**—This condition results from proliferation of the glia about the central canal of the cord, and subsequent necrosis of the new tissue, leaving a tubular cavity.

It has been supposed that the glia cells, or the ependyma cells, are in embryonic condition and hence proliferate freely upon slight irritation, and also rapidly undergo necrosis. Congenital malformations of the posterior wall of the central canal may leave cells belonging to the ependyma or glia in the posterior septum, and these may proliferate later.

With such lesions there are progressive muscular atrophy, disorder of the pain and temperature senses, and vaso-motor and trophic disturbances.

In the gross there may be no marked change in the cord. It may be enlarged, or, with a wide cavity which collapses, it may be slender at one point. On section there may be a dilatation of the central canal, or an obliteration of it by a new growth of glia tissue, which grows also into the anterior or posterior horns and destroys the nerve tissue progressively. The tumor tissue consists of large glia cells with processes, and to these the name of spider cells has been given. Since

the new tissue grows from the central canal and follows the gray matter, it destroys the fibers crossing from the intermediate gray matter to the opposite side of the cord. These are the fibers of pain and the temperature sense.

Continuing to proliferate the tumor will next destroy the tissue in the anterior horns, and hence the paralysis and atrophy of muscles. Such proliferation follows the gray matter both laterally and vertically and thus many segments suffer. In consistence the tumor may be hard if very fibrous, and softer if containing more cells.

*Hydromyelia.* In some cases of congenital hydrocephalus the central canal is widely dilated, with few or no symptoms; this is called hydromyelia.

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## SYSTEMIC DISEASES OF THE CORD.

**Locomotor Ataxia.—Tabes Dorsalis**—In the etiology of this disease, which occurs more frequently in men than in women, and in cities than elsewhere, the chief factor is syphilis. But the disease is termed parasyphilitic, because the lesion is due to toxins from disorders of metabolism rather than to the strictly syphilitic virus. In the juvenile type of tabes inherited syphilis is the indirect cause. Ergot produces similar effects.

The chief symptoms are loss of knee jerk, Argyll-Roberston pupils, fulgurant pains, analgesia and loss of tactile sense, and ataxia. To these other characteristic symptoms are added later in the disease, including arthropathies, perforating ulcer, etc.

The essential lesion is a degeneration in the posterior columns of the cord. In the gross this appears on section as a gray area in the white matter, and its size depends upon the duration of the disease.

The lesion usually develops in the posterior root zones of the columns of Burdach, in the upper lumbar region. In some

cases it begins in the cervical region. With a well-developed lumbar lesion we find also clearly defined wedge-shaped areas in the columns of Goll in the cervical cord, which represent the lower fibers which have passed up.

FIG. 129.

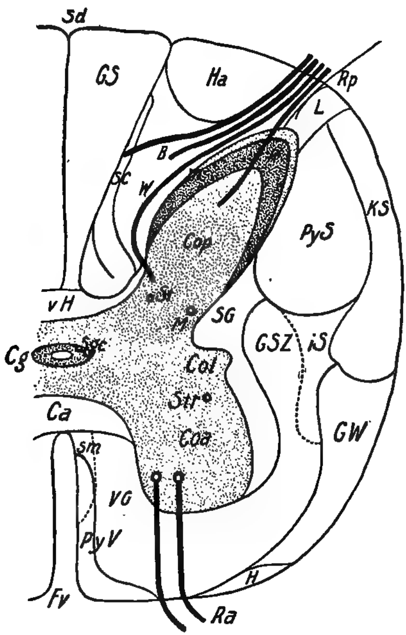


DIAGRAM OF THE CHIEF TRACTS IN THE CORD. (*Obersteiner.*)

*Fv*, ventral fissure; *PyV*, anterior pyramidal tract; *VG*, anterior column; *sm*, sulco-marginal fasciculus; *Ca*, anterior commissure; *Cg*, gray commissure; *Sgc*, central gelatinous substance; *Ra*, anterior nerve root; *H*, Helweg's tract; *GW*, Gower's tract; *iS*, intermediate lateral tract; *GSZ*, mixed lateral tract; *SG*, lateral marginal tract; *Coa*, anterior horn; *Str*, ganglion cells; *Col*, lateral horn; *M*, middle ganglion cells; *St*, Stilling's cells; *VH*, posterior commissure; *KS*, lateral cerebellar tract; *PyS*, lateral pyramidal tract; *Cop*, posterior nerve roots; *R*, gelatinous substance of Roland; *m*, marginal zone; *W*, *B*, and *Ha*, three parts of Burdach's column; *SC*, comma; *GS*, Goll's column, *Sd*, dorsal fissure.

Later in the disease the degeneration involves the entire posterior columns of the sacral, lumbar and cervical regions, except the fibers of the cornu-commissural tract. The lesion extends to the posterior horns and Clarke's columns, and thence to the posterior roots and the spinal ganglia. In some cases a typical parenchymatous neuritis has been observed in the peripheral neurons, both motor and sensory. As a rule, however, the process does not extend to the sensory peripheral neurons, but only to the point where the sheath of Schwann begins.

Degenerations of the intra-medullary portions of the sensory neurons of the cranial nerves have been described. The optic nerve, which is analogous to an intra-medullary sensory tract, frequently suffers parenchymatous degeneration with replacement gliosis.

Several hypotheses have been advanced to explain tabes. Among them are: 1. Meningitis about the posterior nerve roots, causing constriction of their fibers where they enter the cord, and degeneration beyond; 2. Disturbances of the trophic function of the spinal ganglion cells; 3. Proliferation of glia tissue in the posterior columns and secondary degeneration of the nerve fibers; 4. Degeneration beginning in the sensory end organs in the skin and ascending to involve the nerves and the cord.

**Ataxia Paraplegia**, or *combined systemic sclerosis.*—This condition is due to degeneration in both the posterior and the lateral columns, and gives a distinct clinical picture.

The causes are concussion and other injuries of the spine, pernicious anemia, syphilis, lead-poisoning, and, in some cases, malaria. With these apparent causes a predisposition is assumed.

In the gross the cord is atrophic, but the decrease in size is most marked in the region of the posterior and lateral columns. On section of fresh tissue these parts look gray. After hardening in Müller's fluid they are lighter than the rest of the

cord. The tracts most frequently involved are the columns of Goll and Burdach, the direct cerebellar and the crossed pyramidal tracts; Gower's tracts usually escape.

Microscopically a few scattered fibers may be found, but on the whole the nerve fibers, both axis cylinders and myelin sheaths, have disappeared, and their place is taken by glia tissue. When the proliferation of glia is less evident there are many vacuoles, due to the loss of nerve tissue. In these cases the process is considered more acute.

Corresponding to the lesion there are two groups of symptoms, those due to the lesion of the pyramidal tract and those due to degeneration in the posterior column. Hence, as the process commonly begins in the pyramidal tracts, the early symptoms are those of spastic paraplegia; shooting pains, ataxia and other tabetic symptoms are added later.

**Hereditary Ataxia**, *or Friedreich's Disease.*—Beyond the facts that it usually begins about the seventh year and affects more than one of a family, nothing is known of the etiology of this disease.

Nystagmus, disorders of speech, ataxia, choreic movements, and tremors may be present, while sensation and the state of the pupils may remain normal. Scoliosis may coexist.

The entire cord is atrophic, and the columns of Goll and the major part of Burdach's, are degenerated. The cells in Clarke's column are lost. Both the direct and the descending cerebellar tracts are degenerated, and, in advanced cases, the pyramidal and Gower's tracts also. Replacement gliosis occurs in all these situations. It is said that the lesion attacks only such portions of the cord as are functionally connected with the cerebellum.

**Spastic Paraplegia**, or *Lateral Sclerosis.*—This is a degeneration of the central motor neurons and occurs in two types:

1. *Congenital* and *infantile spastic paraplegia.* The commonest causes of the condition are agenesia of the central motor neuron, vascular lesions with atrophy of the cortex,

hemorrhage in the cortex or subdural hemorrhage compressing it, encephalitis involving the cortex of both hemispheres, and syphilis. In the child these lesions may involve but one cerebral hemisphere, giving the infantile type of spastic hemiplegia.

Spastic conditions of the legs, or legs and arms, with marked adduction of the legs, may be noticed soon after birth, and to these symptoms others are added later which point to involvement of the cortex. Among these are strabismus, disturbance of speech from spastic conditions of the speech muscles, epileptic attacks, idiocy, choreic and athetoid movements.

Usually there is a lesion of the cortex, which causes degeneration of the pyramidal tracts, for which the cortical cells act as trophic centers. The cord is small, especially in the region of the tracts. Proliferation of glia is absent or moderate. In the cortex there may be porencephalic or atrophic areas, or microgyria, with small irregular fissures so that the surface of the hemisphere resembles that of the cerebellum.

2. *Spastic paraplegia of the adult.* Syphilis, injury, poisoning, and infectious diseases may precede the attack, which usually develops between twenty and forty.

The disease begins with weakness in the legs and progresses very slowly, with spastic muscles, Babinsky's sign, exaggerated tendon reflexes, no sensory disturbance and no involvement of bladder and rectum.

The lesion is a slow degeneration of the pyramidal tracts, with but little gliosis. The tissue does not respond to Weigert's stain, owing to the absence of nerve fibers.

**Spinal Progressive Muscular Atrophy.**—This disease, of obscure etiology, except that it may follow prolonged muscular exertion, and concussion of the cord, begins after the twentieth and seldom later than the fortieth year.

It begins very slowly with weakness and atrophy of the muscles of the hands, and then spreads to the arms and shoulders and the trunk. In time the atrophy may involve the

diaphragm, or the muscles supplied by the vagus, hypoglossus and glosso-pharyngeus, and thus ends fatally.

The lesion is confined to the peripheral motor neuron. The cells in the anterior horns atrophy, the peripheral motor neuron degenerates, and the muscles change from their normal red color to a yellow. The cells of the muscle tissue degenerate to fatty granular material and this is absorbed, leaving the empty sarcolemma.

The lesion begins in the cervical and upper dorsal cord and spreads up and down in the anterior horns. When it reaches the medulla it affects the nucleus ambiguus and the nuclei of the hypoglossus, facial, abducens and the motor nucleus of the trigeminus. The degeneration in the cells of the cranial motor nuclei gives a group of symptoms which is known as bulbar paralysis.

**Amyotrophic Lateral Sclerosis.**—Contrary to conditions in spinal muscular atrophy, in this disease both the peripheral and the central motor neurons are involved. It occurs between the twentieth and the fortieth years, and follows fright, intense exertion, injuries to the cord, etc., and there may be an underlying hereditary disposition.

Muscular weakness, fibrillary twitchings, and atrophy are noticed in the arms, with weakness and spastic condition of the legs; later all the muscles may be spastic. Tendon reflexes are all exaggerated, Babinsky's sign is present. There is no sensory disturbance and no involvement of the bladder or the rectum. When the disease involves the medulla the symptoms of bulbar paralysis are added.

The cord is very small. The degeneration begins in the sacral and lumbar regions and progresses upward, and has been traced into the centrum semi-ovale. The large pyramidal cells have been found degenerated in the motor cortex. The anterior horns of the cord are atrophic, and their large motor cells are either missing or very small; in the latter case they

stain diffusely and intensely with methylene-blue. The fibers forming the dense network in the anterior horns are fewer than normal.

In some cases the posterior longitudinal fasciculus is degenerated. The nucleus ambiguus and the nucleus of the hypoglossus may be involved. The peripheral motor neuron is degenerated, with atrophy of the muscle cells. The sensory neuron is normal.

The disease is a combination of the lesions of spastic paraplegia and progressive muscular dystrophy.

**Progressive Muscular Dystrophy.**—The disease begins in childhood, very seldom after the twentieth year, and may occur in several members of a family, in different generations. The muscles of the body become atrophic before those of the extremities, and with atrophy in some muscles there may be hypertrophy or pseudo-hypertrophy in others. There are no fibrillary twitchings and the electrical reaction is diminished but not altered in character.

The lesion appears to be confined to the muscular tissue. The primitive fibers of the muscles are either atrophied or hypertrophied, the muscle cells increase in number and the perimysium is hyperplastic. Fat globules appear throughout the muscular tissue and may replace it.

In the *peroneal type* of progressive muscular atrophy, the disease begins in the peroneal group and gradually extends to the arms. Twitchings may be present. There are slight changes in electrical reaction, sensory disturbance is trifling, knee jerks are absent, and pain is usually observed.

Peripheral neuritis and degeneration of the column of Goll, with atrophy of the cells in the anterior horns, may be discovered. In some cases there is a primary lesion similar to that in progressive muscular dystrophy.

## Nerves.

**Inflammation.**—Neuritis occurs as a parenchymatous (or degenerative) and as an interstitial lesion. The former occurs when a nerve fiber is separated from its cell. In about twenty-four hours after the injury the myelin becomes granular and then breaks up into globules; the axis cylinder becomes nodulated and tortuous; the nuclei of the sheath of Schwann enlarge and proliferate. To this entire process, which ends with absorption of the contents of the sheath the name Wallerian degeneration is applied. Regeneration may take place or merely a fibrous cord represents the former course of the nerve. The causes of this condition, which is strictly not an inflammation, are gross injury, intoxications (lead, mercury, alcohol) and infectious diseases (toxins?) as small-pox, diphtheria, typhoid, rabies and others. In some of the diseases which may be due to auto-intoxication or misdirected metabolism, as diabetes mellitus, Addison's and Basedow's disease, and myxedema, similar neuritis may develop. The course of the lesion may be acute but perhaps most often is chronic.

*Acute Interstitial Neuritis* is due to about the same conditions and causes, but the histological process is more correctly called an inflammation. Its type is exudative, the connective tissue being congested and edematous, with pus cells and mononuclear lymphocytes infiltrating it. The gross appearance corresponds, the nerves being red and swollen, perhaps with hemorrhages, yellowish if pus is present in quantity. In its development this process may be hematogenous and affect the endoneurium primarily; or it may extend from the neighborhood and attack the epineurium, as in post-traumatic infection, abscess, etc.

Chronic interstitial neuritis is the sequel of an acute attack or caused by hematogenous or lymphogenous infection and intoxication. Chronic lead and other metallic poisoning, alco-

holism, and unknown factors enter into the etiology; and it may be difficult to decide where the lesion begins, in myelin, or axis cylinder or interstitial tissue. The hyperplasia may be marked in the fibrous elements, and the nervous tissue suffers atrophic and degenerative changes (neuritis interstitialis prolifera); in other cases a good deal of fat is found in the part (neuritis lipomatosa).

**Tumors** of the peripheral nerves may take their origin from the endoneurium or other parts. *Fibroma,* without increase in nerve fibers, and *neuro-fibroma,* with such increase; *neuroma myelinicum,* in which the nerve fibers are medullated, and *neuroma amyelinicum,* in which the opposite is the case; comprise the commonest tumors. *Lipoma, myxoma* and *sarcoma* are infrequent. With multiple neuro-fibromata large areas of the integument may become thickened. This is called *pachydermia neuromatosa.*

# CHAPTER XXI.

## THE LOCOMOTOR SYSTEM.

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### Osseous Tissue.

*Hyperemia* is normal in the bones of the new-born and during their growth. In completely formed bone the marrow is yellow, except in ribs, sternum and pelvis, where a red color persists until late adult life. Pathologically, hyperemia is active with inflammation, passive when the venous return is impeded; if chronic the marrow cells increase and the fat is absorbed. The gross appearances of the bone are redness of periosteum, with swelling and edema, dark or bluish-red color in the marrow, with hemorrhages in some cases.

*Thrombosis* occurs with fracture and from neighboring inflammation, but produces little alteration because of free venous anastomosis. *Embolism,* except of the main nutrient artery and when septic, may also cause no extensive lesion. *Hemorrhage* follows injuries to periosteum and bone tissue, but the blood is usually absorbed rapidly unless infection occurs, as in compound fractures. When a large *hematoma* forms under the periosteum the bone may undergo superficial necrosis from disturbance of its nutrition. One case of such hematoma is found in the new-born, the blood being extravasated under the scalp and periosteum, usually confined to a single bone, as the parietal, from injuries received during protracted and instrumental deliveries. A corresponding hemorrhage between dura and inner surface of the same bone may

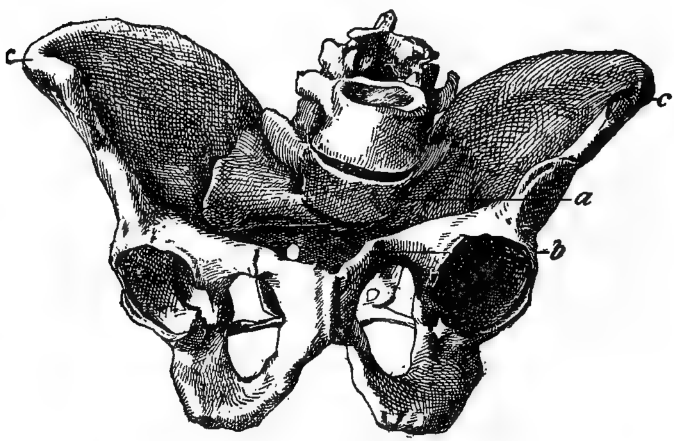
occur. Usually the blood is absorbed without delay. Caries and new growths, especially vascular sarcomata, are other causes of hemorrhage in bones.

**Rhachitis; Rickets.**—This is a nutritive defect in the skeleton connected with insufficient supply of mineral substance to the bones, most always observed in the early years of life (first to third) and associated with anemia, leucocytosis, swelling of the spleen, and intestinal catarrh. While the essential cause of the condition is not definitely known, it may be that the chief factor in its causation is excessive formation of lactic acid in the alimentary canal, imperfect absorption of lime salts, and deficient alkalization of the blood, together with imperfect oxidation in the tissues. The excretion of mineral matter by way of the kidney may be excessive, but usually it is below normal. All parts of the skeleton, and both the periosteal and the medullary aspects of the bones, show imperfectly ossified tissue, and the usual arrangement in concentric layers in the long bones is imperfect or absent. In the epiphyses the deposit of lime salts is irregularly distributed or lacking. In some cases there is large formation of osteoid tissue under the periosteum, especially at tendinous and aponeurotic insertions. The marrow is generally red and rich in cells, resembling the fetal condition; the vessels at the epiphyseal ends may be actively congested. The enlargement of the ends of long bones is due to the hyperplasia of cartilage cells, increase in size in the medullary spaces, and development of osteoid tissue, together with the effects of gravity and pressure. The common deformities which result are bendings of long bones (infractions), swollen ends in ribs and limbs, large cranium with prominent forehead and open fontanelles, spinal curvatures (*kyphosis* if backward, *lordosis* if forward, *scoliosis* if lateral; these may be combined), and prominence of the sternum (pigeon breast). In the pelvis the deformity is important in relation to child-birth; the commonest change, from muscular traction and superposed weight, is shortening of the superior

conjugate diameter and lengthening of the transverse. When the sacrum is specially prominent the inlet has a trefoil outline.

A prenatal rhachitis occurs in which the bones are uniformly thickened and shortened, with large ends, bendings, and adipose hyperplasia under the integument, and sometimes cretinism from premature union of the cranial sutures.

FIG. 130.




OSTEOMALACIA OF THE PELVIS. (*Ziegler.*)

*a*, last lumbar vertebra, displaced forward; *b*, horizontal ramus of pubes, bent backward; *c*, iliac crests.

**Osteomalacia** is a disease of adult life, commonest in women, in connection with parturition, in which there is rapid and general resorption of the inorganic salts from the bone. A mild degree of decalcification appears to be frequent in puerperal women, and the disease has been regarded as a tropho-neurosis associated with pathological excess of this process. It occurs in certain regions especially (along the Rhine). It may be limited to special portions of the body (pelvis), or begin

thus and involve other bones in succeeding pregnancies. The prognosis is almost invariably bad.

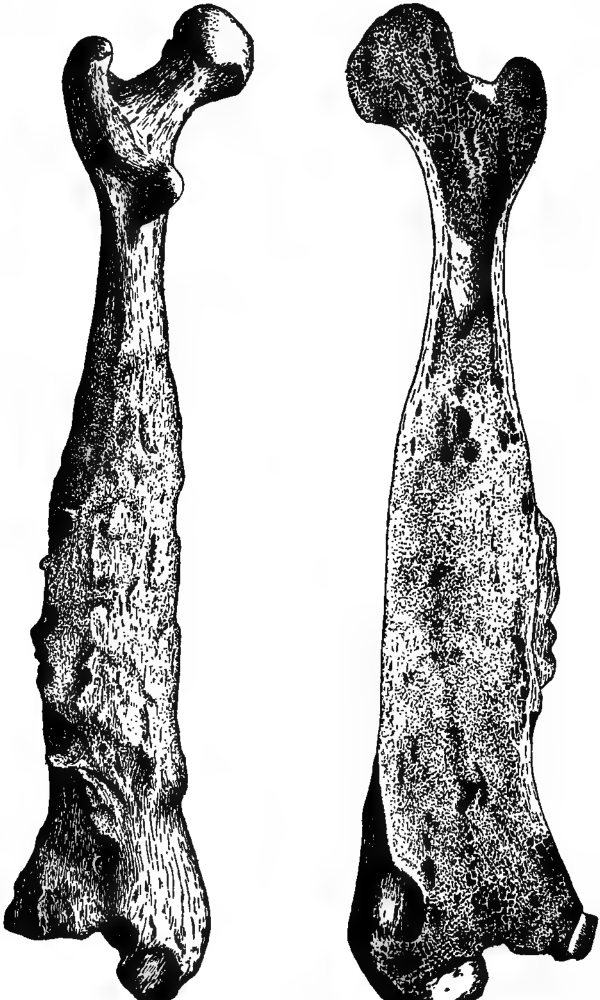
Spongy bones suffer most but the lesion, with fractures and deformities, is not confined to them. In the pelvis the pubic arch and the sacral promontory are pushed forward, the iliac crests outward and the sides of the pelvis inward, resulting in a beaked and triangular pelvis. Owing to spinal tenderness the patient lies habitually on one side, with consequent unilateral excess of the pelvic deformity. Fractures are common and multiple, occurring spontaneously or with slight injuries, and as many as thirty in one patient have been recorded. Since the process begins in developed bone its structure is retained for a time, even when soft enough to cut, but in fractured parts and bent bones osteoid tissue is common, not in regular arrangement. The fractures show a tendency to repair even during the activity of the process of resorption.

In the gross the bones are soft, may be freely bent and twisted, cut easily with a gritty feel if still containing salts. Layers of osteoid material under the periosteum and in the medullary spaces are found, the marrow is congested, fatty or gelatinous. Calcified and soft parts may be sharply distinguished from each other or gradually fade from one into the other. Microscopically the Haversian canals are widened, new fissures form, the decalcified tissue is fibrillar with perhaps a trace of lamellar arrangement, and the bone corpuscles are atrophic. The marrow may be hyperemic, rich in cells, or in a condition of mucous degeneration. Osteoid tissue may contain large bone corpuscles.

General cachexia sooner or later appears and the patient dies of pneumonia or other intercurrent disease.

**Inflammation.**—*Periostitis* may be simple, suppurative or productive (ossifying). Simple or fibrous inflammation results from contusions and other non-infected wounds and produces general thickening of the membrane, with firmer adherence to the bone. Inclusions of foreign matter may result in such

FIG. 131.



CHRONIC OSTEITIS AND PRODUCTIVE PERIOSTITIS. (*Coplin.*)
Surface of bone under periosteum nodular and thickened, marrow cavity nearly obliterated.

inflammation long after the injury is received. The vicinity of chronic ulceration (leg) and joint affections commonly results in such fibrosis. The periosteum appears hyperemic and swollen and infiltrated with round cells.

*Ossifying periostitis* is a chronic process which results in the production of exostoses, osteophytes and bony thickenings. It may invade connective tissue adjacent (parosteitis). The usual condition with which this form is associated is chronic inflammation of joints, syphilitic and other disease of bones, but it may appear with general constitutional diseases (rickets) and physiological states (as bony plates in the dura with pregnancy). The toxins of chronic tuberculosis seem at times sufficient irritation to cause it.

*Purulent periostitis* may result from infection through the blood or directly from bone disease; pyogenic organisms of all varieties are found. A circumscribed form with abscess under the membrane may lead to exfoliation of a thin sheet of necrosed bone, with perforation externally and extrusion of the sequestrum. At times the condition is so general and destructive that the name *periostitis maligna* is given to it. The process may lead to suppuration in the medullary canal or result from it, and in either case the danger of septicemia and pyemia is marked.

*Osteitis and Osteomyelitis.*—These two conditions can hardly exist separately. The cause is usually infection and the course is either acute or chronic, the former producing abscesses and the latter a fungous condition from excessive granulation tissue, abscess and necrosis. Acute traumatic inflammation follows fracture with infection, amputation and other injuries, and causes hyperemia and swelling of the marrow, diffuse infiltration with pus, and abscesses where this is most evident. Necrosis and sequestrum formation, perforation of the pus into joints or outwardly, and pyemic infection may be associated with this form. Acute infectious (spontaneous) osteomyelitis occurs chiefly in the long bones, hemorrhages may

occur, the epiphyses may separate or even an entire bone undergo necrosis. In less extensive cases single abscesses may form in one bone. Pyemia is the common end of the worst cases.

Chronic inflammation of the bones is usually associated with preceding acute disease of the part, wounds, syphilis and tuberculosis; specific forms show the usual caseous changes. A rarefying form is described (*osteoporosis*) and a condensing form (*osteosclerosis*). The former is accompanied by absorption of the walls of Howship's lacunæ by osteoclasts, which begin as small cells and end as giant cells, sometimes with processes, and cause chemical destruction of the gelatinous elements of the bone and absorption of the lamellæ. A reparative or reactive osteosclerosis is often associated with the foregoing and may cause deposit of new bone under the periosteum (eburnation) and also fill the medullary canal with it.

*Necrosis.*— Embolism of arteries, separation of the periosteum, inflammation of various portions of the bone, may lead to such nutritive disturbance that a portion of it dies. This process is called necrosis and the dead piece of bone, the *sequestrum,* is partly softened and absorbed, the remainder lying as an irregular eroded body in a cavity lined with granulations and partly filled with pus. The pus makes its way through the thickened periosteum and discharges on the surface through one or more fistulæ or sinuses, bits of dead bone coming away also. The granulating periosteum begins to form new bone about the sequestrum, which lies as a foreign body under it, but complete repair can follow only when the sequestrum is cast off. In necrosis of the central parts of the bone this is usually difficult. When it occurs in a stump after amputation, a ring of bone with lateral projections into the marrow cavity may be formed and be easily removed. With chronic phosphorus-poisoning necrosis of the bones of the face, most commonly the lower jaw, begins in the periosteal aspect of the bone and is accompanied by production of new osseous

tissue. Suppuration is common and may lead to pyemia. After operative removal the patient may recover with much distortion of the parts. The entrance of phosphorus vapors and pyogenic organisms is facilitated by caries of the teeth.

*Tuberculosis of Bones; Caries.*— Miliary and other forms of tuberculosis occur in the bones, before birth, in childhood, and less frequently in adult life with lung lesions. The disease is hematogenous, the bacilli brought through the blood-current, and secondary to tubercular lesions of the lymph nodes (scrofula) and the organs of the thorax and abdomen; in the child, portions of bone in most active development are involved and previous injury is often recorded. The disease often begins in spongy tissue at the ends of long bones and opens into the joints, or in the small bones of the hands and feet.

In the gross there are small grayish or yellowish foci, singly or in groups, surrounded by a margin of active hypermia. These increase in size, become confluent, and undergo caseous softening of their centers, the portion of tissue involved may separate from the still healthy bone by a line of demarcation, and within it occurs the molecular death of the tissue known as caries, in distinction to the large sequestra of necrosis. The focus of softened bone, mixed with pus, forms a tuberculous abscess, its walls covered with a pyogenic membrane. The combination of rarefying osteitis, granulation-tissue formation to replace the lost bone, and destructive suppuration of this, progresses in the line of least resistance and opens into joint cavities or externally, usually by multiple sinuses. The pus focus in rare cases becomes encapsuled, thickened and healed. Should perforation of the pus follows the lines of muscles and fascia (as in caries of vertebræ) the sinuses lead for long distances through the tissues and permit the accumulation of large amounts of pus. To these the name cold abscess is applied, and in psoas abscess, one of the commonest, the entire integument above the knee may be elevated from the muscles and converted into a sac filled with pus. It is especially in the

long-continued suppurations connected with chronic osteitis that amyloid degenerations of the viscera occur

*Syphilis.*—Congenital syphilis occupies especially the epiphyseal lines of the long bones, appearing as a pale yellow jagged line about 2 mm. broad; this increases in width as the cartilage adjoining it becomes swollen and gelatinous. Later the fatty degeneration of the cells between the line and the bone permits the easy separation of the epiphysis. The spleen is commonly enlarged in this disease.

Acquired syphilis causes periosteal growths, and gummatous infiltration with softening and necrosis, leading to large defects in the bones (as of the skull), and condensing osteitis.

*Leprosy* causes severe ulceration of the soft parts and necrosis of the underlying bones (*lepra mutilans*) which ends in loss of large portions of the extremities. Other bone lesions in this disease are osteomyelitis, and granulomata with giant cells and lepra bacilli in the marrow.

*Atrophy.*—The process of absorption and replacement of bone is constantly present during life. In marasmus, cachexia, senility and lack of use the replacement may reach so low a proportion that the bones atrophy, generally or in special regions. The localized atrophy occurs from pressure, as with aneurysm and tumors, because the periosteal vessels are occluded, and the nutrition, both of the membrane and the bone, prevented. The general form occasionally occurs in young subjects, often in more than one of a family, without apparent explanation. General atrophy is also called *fragilitas ossium.*

In certain injuries the bones of a part, as a limb, become useless, and in early life they may remain behind in development (hypoplasia); as a congenital defect this hypoplasia produces dwarfs (*microsomia*).

*Hypertrophy* as a general condition of the bones, seems, like general atrophy, to be connected with trophic nervous centers. The most marked instance of this is acromegaly, a pathological giant growth developing most often about puberty, leading to

excessive size of the limb bones, extremities, and face. With this condition syringomyelia and lesions of the pituitary body have occurred, but a causal relation has not been established between nervous lesions and the condition.

Local hypertrophies occur as exostoses, osteophytes, and exercise bones. Some of them are due to irritation of the periosteum, and some to hyperplasia laterally from epiphyseal cartilages. If chiefly composed of cartilage the tumor is called *exostosis cartilaginea,* if of bone, *osteoma.*

**Tumors.**—*Fibroma* and *myxoma* may affect the periosteum; chondroma and osteoma are the commonest benign tumors of bone.

*Sarcoma* occurs as a primary tumor in most of its forms, peripheral or central, including spindle-celled, round-celled, pigmented, angiosarcoma and giant-celled. The growth causes resorption of the bone, breaks through the periosteum and reaches a large size; where the periosteum is preserved a new deposit of bone goes on from its under side so that the tumor is enclosed in a thin shell. On scraping the fresh section a milky fluid may be obtained, which presents spindle cells and branching forms, when examined in salt solution. It may grow slowly for years, without affecting joints or making metastases or causing much pain. General sarcomatosis of many bones may occur but this is usually secondary to a distant neoplasm. Microscopically the cells are distinguished from marrow cells by their uniform size, their finely granular protoplasm, the appearance of spindle cells, and rapid invasion of the tissues. A special variety of sarcoma of the periosteum of cranial and facial bones is called *chloroma,* from its green or yellow color.

Primary *carcinoma* of the bones probably never occurs; as a secondary tumor all varieties have been observed. Epithelioma of the skin may directly invade subjacent bone, with progressive absorption. Embolic cases of multiple development have been called carcinomatous osteomalacia.

*Cysts* occur in bones almost entirely from softening of other neoplasms, as myxoma.

In leukemia and pseudo-leukemia the marrow may present numerous small lymphoid tumors, called *lymphoma* or *myeloma*.

## Joints.

**Injuries and Displacements.** — Fractures may lead into joints. Pieces of articular cartilage may be broken off and remain as foreign bodies in the joint cavity (floating cartilage, as in the knee). Complete solution of the relations of bones at joints is called dislocation; incomplete forms are called subluxations. The capsule of the joint and one or more of the ligaments are torn in such injuries, as also the tendons, muscles and other structures about the joint. When the relation of the bones is restored, healing in the capsule and ligaments rapidly follows by productive inflammation. If unreduced, the end of the bone suffers partial absorption, ossifying periostitis makes a new false joint and fairly good movement may be possible; the torn muscles and ligaments atrophy. In other cases the bones are united more or less firmly by fibrous, cartilaginous or bony tissue, with practically no motion preserved and no attempt to form a joint; the condition is known as ankylosis. It occurs also as one of the results of inflammation in joints.

*Hyperemia* of a joint may be the only appearance at autopsy corresponding to acute rheumatic affections in the early stages and after contusions. The edges of the cartilages and the synovial membrane present swollen vessels or even hyperplastic increase (*synovitis pannosa*) and the fluid of the part may be increased.

*Hemorrhage* into joint cavities (*hemarthros*) is usually the result of injury, but it occurs also in hemorrhagic small-pox and other constitutional conditions; the blood may be absorbed or leave pigment granules in the tissues.

*Edema* (*hydrarthros*) occurs with inflammation, almost never with hydremic conditions.

**Inflammation.**—*Fibrinous arthritis* may be "dry" or accompanied by extravasation of serum. It exists as one of the lesions of articular rheumatism, or with inflammation in the vicinity of the joint, or after traumatism. The fibrin lies in the fluid as white or yellowish flocculi or as a film clinging to the synovial surfaces. With the addition of pus the forms of arthritis known as sero-purulent and fibrino-purulent occur; it is commonly the case that all three elements appear together, as with infectious diseases. The synovial membrane is thickened and swollen and covered with soft layers of purulent fibrin; all the tissues of the joint are infiltrated with pus-cells. If the joint contains chiefly pus the name *arthropyosis* or abscess of the joint is employed. The common result is the destruction of the cartilages, and caries of the articular ends of the bones; the ligaments and tissues about the joint are also involved (*panarthritis*). After the pus escapes, healing with ankylosis may occur, or chronic inflammation persists with its danger to life from pyemia and amyloid degeneration. Such joint abscesses at times complicate typhoid fever, diphtheria and dysentery, and are common in pyemia.

*Chronic arthritis* includes several forms of inflammation of the joints with secondary atrophic changes, and others in which degeneration is more evident than inflammation. The etiology may be the same for the two; preceding inflammation, injury, anomalies of metabolism, senility and certain central nervous conditions are the chief factors. Chronic arthritis appears both with and without exudation.

Chronic serous arthritis (*hydrarthros*) follows serous and sero-fibrinous acute lesions or begins as a chronic condition, as in the knee. The synovial membrane is swollen and opaque, its edges proliferate, and the joint contains a varying amount of serous fluid. The usual course is a transition to one of the other forms of chronic arthritis.

Chronic suppurative arthritis is the result of infection through the blood or from abscess in the neighborhood; it may follow acute suppuration and is common with tuberculosis of the joints. The synovial membrane is thickened and covered with purulent fibrin, the cartilages undergo fatty degeneration, their basement membrane becomes fibrillary; necrosis follows and exposes the bone, which then becomes inflamed. In favorable cases the joint becomes rigid as the process is healed.

The non-exudative forms of chronic arthritis include arthritis deformans, arthritis sicca, arthritis adhesiva, a fungous form with tuberculosis, and uratic or gouty arthritis.

*Arthritis deformans,* chronic gout or rheumatoid arthritis, includes chronic degenerative with productive lesions, and results in such alterations as to merit the name deformans. Its course covers years and usually begins in late adult life. The first changes are in the cartilages, the basement membrane becomes fibrillary and the cells proliferate actively; afterwards fatty degeneration destroys the cartilages, especially at the sides of the articular surfaces. The bone thus laid bare becomes hard and polished, but already, under the remaining cartilage, the bone has undergone marked absorption. The ligaments, at first thickened, become contracted and fibrous, and, together with the production of new bone about the edges of the joint, help to produce complete ankylosis. The absorption permits luxations, and the ankylosis often forms afterward. The hip, knee and finger joints in this way may present every variety of dislocation and every angle of ankylosis, rendering the patient entirely helpless.

*Arthritis sicca* differs from the preceding but little; it is common in the aged, attacks the hip, shoulders and elbow in the order of frequency, and is not connected with such destruction of bone and production of new osseous tissue. The arthropathies seen with tabes dorsalis and syringomyelia resemble arthritis deformans of more than commonly slow progress and may involve only the lower extremity.

*Adhesive arthritis* follows acute and other inflammations and leads to the union of joint surfaces by the production of organized fibrous tissue starting in remnants of cartilage, especially where the amount of exudate has been small. Many joints may be affected at once. From the large amount of vascular new formed fibrous tissue the process is sometimes called arthritis pannosa.

*Arthritis uratica,* gout, podagra, follows from the deposition of urates in the fibrous connective tissues about joints, in the cartilages and the bones, and commonly affects the small joints of the hands and feet, especially of the big toes. Similar deposits occur in other places. Beside the joint lesion there are commonly visceral and vascular changes associated, fatty heart and liver, chronic interstitial nephritis, gravel and calculi in the urine, tophi in the external ears, and arteriosclerosis. The course of the disease is very chronic, marked by periods of a few days of acute and painful inflammation of the joints (the paroxysm) and months of apparent health. While the etiology is not definitely understood, the disease attacks by preference those who live well, consume wines habitually and take but little exercise. The soluble quadriurates circulating in the blood become changed into the insoluble biurates and are deposited about the joints, perhaps with some relation to the habitually low temperature and the exposure to injury of these parts.

*Tuberculosis* of the joints follows rupture of a tuberculous bone focus into the cavity, or it begins as a primary fungous synovitis (synovitis granulosa). While bacilli are present in all acute cases, it is sometimes difficult to find them, except by inoculation of animals from the joint contents. The joint affected is swollen, edematous and altered by luxations. On section the tubercular masses may be found as gray or yellow points. The joints may be filled with profuse granulations, or they may have suffered purulent softening and the bone is the seat of caries; cold abscesses developed in this way may remain till the joint is practically disorganized, or burrow and

empty on the surface. Where the joint supports weight, as in tubercular diseases of the vertebræ (spondylitis), kyphosis, and other deformities result. The disease frequently develops in children, with or without injury to the joints, and the larger articulations are specially liable to invasion, as the hip, knee and elbow. Favorable results with ankylosis are obtained in some cases, but the position of the limb is seldom normal. "White swelling" was the name formerly given to this disease in the knee.

*Syphilis* in the congenital form thickens the capsules and ligaments of various joints, or a gumma near by may soften and involve a joint, or syphilitic osteochondritis may become a purulent lesion and invade the joint and the tissues about it. In adults gummata may form in joints and by their softening and scars produce an arthritis deformans syphilitica.

**Tumors.**— From the synovial fringes small lipomata and fibromata develop and on separation they may be free in the joint. Another and more numerous newly formed body in joints is the so-called rice-like bodies, which occur also in bursæ, fifty or more at a time. They probably arise from hyaline portions of the synovial membrane. Other neoplasms occur in connection with bone lesions.

## Muscles.

*Anemia* is part of a general condition or results from local pressure and loss of circulation; the muscle is pale and dry at first, later it shrinks and becomes friable.

*Hyperemia* is physiological with exercise, and occurs with inflammation; stasis is unusual. All these conditions are difficult to appreciate on the dead subject owing to the changes of the death agony and rigor mortis.

*Hemorrhages* occur from tears and contusions, and after degeneration of the tissue, as with waxy muscles in typhoid. Thrombosis and embolism are not important here.

**Inflammation**, myositis, follows injury and infection; the organisms may come from the vicinity or by the blood (pyemia).

*Acute myositis* with serous exudate, inflammatory muscular edema, is accompanied by an edematous affection of the connective tissue between the muscle bundles with cellular infiltration to a moderate degree, while the muscle cells remain nearly passive or degenerate, with vacuole formation and hyaline changes. It follows injury, external or caused by trichinæ and anthrax. The fluid may be absorbed, or purulent and hemorrhagic features be added.

*Acute primary polymyositis* is spoken of when many muscles at once are attacked, without apparent cause. The muscles swell and become extremely painful and tender, and the skin over them may be edematous. The function of the muscles involved is important; if those of respiration and deglutition are affected, death by pneumonia may speedily result. The muscle is pale or streaked with yellow, and under the microscope shows irregular cell infiltration between the fibers and the bundles. The striation of the muscle is lost, fatty and granular changes occur and fissures in the muscle fibers. The apparent resemblance to toxin effects is noticeable but no bacterium has been discovered.

Secondary acute myositis may occur with infectious disease (variola, typhoid and diphtheria).

*Hemorrhagic myositis* may be the result of extension of diphtheritic inflammation from the margins of a tracheotomy wound, or result from extension of phlegmonous inflammation of other parts. Scurvy and serpent venom may also cause it.

*Acute suppurative myositis* usually occurs as abscesses in the interstitial connective tissue. Their origin is traumatic, embolic and pyemic, or cryptogenic. A phlegmonous form results from severe skin lesions and extension to the muscles below. The results differ with the infection; in mild cases

the perimysium offers an obstacle, in others the suppuration invades the muscle and abscesses form.

*Chronic myositis* may be a slow purulent lesion without apparent reaction (cold abscess) with chronic tuberculosis, actinomycosis and glanders. Or it may be a slow productive lesion, with increase in the fibrous (*myositis fibrosa*) and atrophy of the contractile elements, as after acute myositis, after neuritis and other nervous lesions and in the vicinity of chronic bone and joint diseases. Or, thirdly, it may be of the ossifying type, localized at tendinous insertions, from prolonged activity of the muscles (exercise bones, etc.). A progressive myositis ossificans sometimes occurs in the young after severe falls, chilling of the surface and sudden efforts, involving the muscles of the back and neck and resulting in wry neck and other deformities from permanent shortening.

*Tuberculosis* of muscles occurs as cold abscess in connection with joint and other lesions; other forms are unusual; even with general miliary tuberculosis the muscles are commonly not affected.

*Syphilis* causes a fibrous myositis, with contractions, and usually involves one or but few at a time (masseter, biceps); or it occurs as gummatous infiltration, sometimes of a single muscle, as the sternomastoid of one side.

*Glanders* invades the muscles as multiple small foci or nodules with a tendency to suppurate and break down. It may extend from the mucous membranes, as of the mouth, or be generally disseminated.

*Atrophy* may be simple, myopathic or neuropathic, according as it depends on defective nutrition, disease of the muscles, or central nerve lesions.

Simple atrophy occurs in old age or when muscles are not used for long periods, as in fractured limbs in splints.

Primary myopathic atrophy may develop in childhood and there appears to be a strong hereditary history with many cases. Several muscles at a time may be involved, usually in

the lower extremities, as the calf. The actual size of the part may be larger than normal owing to the fatty replacement (lipomatosis), but the muscle cells are atrophied, with here and there a large fiber. No demonstrable changes in the nervous system occur in this form, which is one of the chief reasons for separating it from the next.

Muscular atrophy of neurotic origin may result from the most diverse lesions in the cord. Syringomyelia, lateral sclerosis, descending degeneration after cerebral lesions and multiple neuritis, are some of the conditions in which the muscles atrophy in the territory of distribution of affected nerves. So-called progressive muscular atrophy as a clinical entity begins often in the small muscles of the hand, proceeds to involve those of the forearm, upper arm, shoulder, diaphragm and back, and may not at all affect those of the lower limbs. Atrophy and degeneration of the muscle fibers, fibrosis of the interstitial tissue, and fatty degeneration in the nerves of the part (motor) are the usual conditions found. The anterior nerve roots and the anterior horns of the cord may also present evidences of degeneration with atrophy of the ganglion cells. This is most marked in the cervical enlargement, corresponding to the muscles most involved.

*Hyaline* or *waxy degeneration* of the muscles occurs in the course of infectious diseases, especially typhoid fever, and while any muscle may be involved, even the heart, the rectus abdominis is most often the seat of the process. In the gross the muscle is dry and glistening, with stripes of granular or hyaline degeneration, and has a waxy look. Microscopically the fibers are first swollen and then homogeneous and dull; transverse fractures occur, as also in the gross; hemorrhage may take place into the tissue of the muscle. Fibers not waxy present granular changes and the interstitial tissue is hyperplastic. Of the many other diseases besides typhoid in which this change occurs, may be mentioned burns and freezing, delirium tremens, progressive muscular atrophy, neoplasms invading muscles, trichinosis, small-pox and relapsing fever.

*Fatty degeneration* occurs with myositis and any cause which deprives the muscles of nutrition. Two special forms are worth mentioning, that occasioned by phosphorus, which seems particularly to affect the trunk muscles, and a similar condition in the new-born, chiefly limited to the lower extremities.

In obese persons a form of fatty infiltration occurs.

The most important parasite in muscles is the trichina already described in Pt. I., p. 203.

## Tendon.

*Inflammation* (thecitis, tendo-synovitis) follows injury or extends from suppurating foci along the course of the tendon. Its course may be acute or chronic and the exudate may be chiefly serous, fibrinous or purulent; the results are much the same as in the case of arthritis with exudate.

*Tubercular disease* of the tendons usually results from similar lesions of bones and joints in the vicinity. The sheath of the tendon is usually much thickened and in the secretion rice-like bodies are often found in numbers.

*Ganglion* is the name given to a collection of fluid in the sheath of a tendon, or in a hernial protrusion of it, and the fluid is serous or more gelatinous.

*Bursitis* affects principally those bursæ which are situated in front of bony prominences subject to constant pressure, as in miner's elbow, coachman's bursa, housemaid's knee. As is evident from the popular names, the condition is a lesion of occupation. In the old days of the hand loom, "weaver's bottom" was a common complaint, from inflammation of a bursa over the tuber ischii. The inner surface of the thickened bursa is usually smooth, lined with flat cells, or roughened, and the fluid is either serous or purulent. Fine vegetations occur in the chronic form and rice bodies (*corpora oryzoidea*); these are regarded as tubercular by some writers.

Tuberculosis and tumors involve the bursæ and tendons from the accident of vicinity.

# CHAPTER XXII.

## THE SKIN.

Disease processes are the same here as in other organs but their effects, owing to local conditions, are much more varied. The skin is not only exposed to extremes of heat and cold, to which other viscera are not subject, but it is the habitat of many parasites from whose invasion the internal organs are free. Moreover its structure is complex and the same morbid condition in different situations may produce pathological and clinical pictures of wide variance. Even in the same location, a toxic agent may cause several alterations which have little in common. It is necessary to recall one point in physiology, that the sweat glands secrete a fluid fat, in addition to water holding various salts in solution, while the sebaceous apparatus produces only a solid fat for the lubrication of the hair.

As they recur constantly, it is well to begin with a perfect understanding of the cytological terms employed here. In addition to the ordinary elements found in exudation, the polynuclear leucocyte, eosinophile and lymphocyte there is at least one other of importance, the plasma cell. This last is a derivative of the lymphocyte probably and shows a round, eccentric nucleus whose chromatin stains in clumps, not diffusely, and basophile protoplasm (methylene blue) more dense at the periphery. The cell is ovoid or polyhedral from pressure. Cells derived from the fixed connective tissue corpuscles are of several sorts; the fibroblast with oval, vesicular nucleus, branched or spindle-shaped body whose protoplasm is granular and gen-

erally slightly basophilic; the pseudo-plasma cell (sometimes called connective-tissue phagocyte) which differs from the plasma cell in being larger and in having a homogeneous protoplasm with affinity for acid dyes; the epithelioid cell which is oval, acidophile, with a large vesicular nucleus; and the mast cell whose origin in doubtful. The last occurs in bizarre forms but it has a distinctive characteristic in that its granular protoplasm exercises a selective action on the red in Unna's polychrome methylene blue. Giant cells, also fibroblastic in origin are of two types, the myeloid whose nuclei are scattered through the cell body, and the Langhans form, in which nuclei occur in a peripheral horseshoe or ring.

For convenience, the classification used by the American Dermatological Association will be followed here, omitting those disorders whose rarity makes their consideration suitable only to works on dermatology, and others, like the neuroses, which leave no demonstrable histological traces.

**Anomalies of Secretion.**—Anomalies of secretion comprise those evidenced by changes in composition and in amount, increase or decrease. Cysts are not strictly part of this category but may as well be considered here since the secretion forms the tumor.

*Bromidrosis* is due to contamination of the eliminated sweat by the bacillus fetidus, the offensive odor being due to the by-products of its activity. *Chromidrosis*, blue, red or green sweating, owes its appearance to various chromogenic organisms. *Uridrosis* is the result of the elimination through the skin of the urinary salts. Suppression is not a necessary precedent. *Hematidrosis* occurs in hemophilia and in psychical disturbances where stigmata appear, blood-corpuscles or hemoglobin being present. *Hyperidrosis* is often congenital and may display a striking unilaterality, occasionally in the distribution of a single nerve. Many observations point to a purely nervous origin for it. *Anidrosis* is never total and occurs in the course of systemic disease. *Seborrhea* was formerly thought to

be an anomaly of sebum secretion but is now recognized generally as a part of seborrheic dermatitis. So far as is known there is no qualitative change in the product of the sebaceous glands.

*Sudamina, hidrocystoma* and *miliaria* are retention cysts occurring along the tract of the sweat ducts. Sudamen and miliaria are superficial, hidrocystoma rather deep in the corium. Sudamina occur in the course of fevers, are located chiefly in the epidermis, whose layers are separated by the fluid, and are accompanied by little inflammation. Hidrocystoma has a thick covering composed of the whole epidermis with part of the papillary layer. The duct is enormously dilated in its middle third as a rule and the cavity may be lined by flattened cells. Miliaria is the ordinary "prickly heat," and differs from sudamina in being an inflammatory lesion. All three occur in conditions of excessive moisture and high temperature, hidrocystoma almost exclusively on the faces of washerwomen and cooks. The sweat duct has no lining of its own in the epidermis, consequently the moisture causes the cells to swell, the lumen is finally blocked and a cyst results, superficial or deep as the obstruction occurs in the horny layer or among the prickle cells. In long periods of tropic heat miliaria may become pustular, pyococci finding a suitable medium in the warm, sodden skin. They may be introduced from outside or, living in the organ, like the staphylococcus epidermidis albus, merely awake to activity. Fatty, sudoriparous cysts occur outside of these conditions, in males at the time of puberty. They are probably due to a congenital defect of patency in the sweat apparatus. The water excreted is doubtless reabsorbed, leaving a semifluid fat. The cysts are subject to infection. Ducts have been traced into all these cystic formations.

Milia and sebaceous cysts differ as do sudamina and hidrocystoma, in their location in the skin. The former never attain great size and are superficial; the latter are large and deeper.

Both are caused by obstruction, congenital or acquired (scar), in the sebaceous opening. The epithelial cells of the lining are flattened or disappear and the solid, fatty mass is enclosed in a thick fibrous capsule. The pressure of the cyst causes atrophy of surrounding structures and thinning of the epidermis. The contents may calcify after a lapse of years.

## Inflammation.

*Urticaria.*—The characteristic lesion of urticaria is the wheal, due to rapid outpouring of serum from the superficial vessels. In susceptible individuals the vaso-motor apparatus is in a state of unstable equilibrium and responds at once to slight stimuli, external, internal and reflex. On the first application of the stimulus the vessels dilate and a large amount of serum is exuded, relatively to the area involved. If the tissues are loose, the lesion remains red; otherwise, the fluid in the interstices causes a compression of the blood channels and the center becomes white. In children, rarely in adults, the exudation may be sufficient to raise the epidermis and form a bulla. The efflorescence requires only a few minutes for its evolution and its subsidence may be quite as rapid, so that there is no opportunity for alteration in the epidermis or proliferation of fibroblasts. Serum is not the only blood element exuded. In dermographism, or factitious urticaria, there is an extravasation composed entirely of lymphocytes which is present in a slight degree in the ordinary form. Urticaria is hemorrhagic at times from diapedesis of red corpuscles. The mechanism of giant urticaria, or angioneurotic edema, is exactly the same as in the smaller wheal, the area involved reaching great size.

*Erythema.*—This term is applied to a number of conditions, but here its meaning is confined to Hebra's erythema exudativum multiforme, a name which describes the condition closely. Multiform erythema is ultimately allied to urticaria

and purpura rheumatica. Its basis seems in most cases to be a condition identical with that known as acute rheumatism. This erythema is a symptom of a systemic intoxication which may produce also gastro-intestinal crises and acute nephritis. Pyococci have been cultivated from the skin and blood in many cases. Drugs often cause an erythema.

The histology of this lesion is simple. There is dilatation of the vessels of the corium and an extravasation about them, composed chiefly of polynuclear leucocytes with an edema much less marked than in urticaria as a rule. There is little alteration in the epidermis but in persistent cases there may be some overgrowth in it. In the papular form, leucocytic invasion is the striking characteristic; in bullous erythema, edema is sufficiently great to raise the horny layer; in herpes iris, the bulla subsides in the center, leaving a ring peripherally, containing fluid; in erythema nodosum, there seems to be a total vessel paresis, the lesion is blue from stasis, boggy from edema and on subsiding leaves discolorations like a bruise. In addition to organisms often present, there is an eosiniphilia of the serum in the bullæ which is very rarely found in the blood. In purpura or peliosis rheumatica, in addition to the usual picture present in erythema, there is extensive cutaneous hemorrhage, red corpuscles occurring intact or partly destroyed. Hemorrhage occurs in the course of erythema not infrequently as the result of administration of salicylates, a condition which should not be mistaken for purpura in which hemorrhage is the chief symptom.

## Scaling Dermatoses.

In inflammations of longer standing than the two just considered, when the process is of a subacute or chronic character from the beginning, changes occur in the epidermis which are charactertistic of all cutaneous catarrhs, moist or dry. All of them are directly attributable to the presence of an increased

amount of serum, an edema, of the epithelial layer. The first change is a widening of the intercellular spaces, intercellular edema or spongy metamorphosis, as Unna calls it. The second is an intracellular edema, due to imbibition of the fluid by the cells which favors a retention of their juicy, granular character normal in the lower layers up to the surface, the clear and horny layers having disappeared. The edema prevents a proper transformation of the cell-protoplasm through keratohyalin into the keratin of the horny layer, and the cells, instead of desquamating as in normal conditions, stick together and a scale is formed. This process is called parakeratosis, is present in every scaling disorder, and is not to be confounded with hyperkeratosis in which the horny layer is greatly thickened but the cell transformation is complete. The third phenomenon is overgrowth of the rete. Its interpapillary projections are widened or lengthened or both and the whole layer is increased in depth. Mitoses are to be found in the germinal or palisade cells. The condition is called acanthosis. All are secondary to inflammation of the corium.

*Eczema* may with entire justice be defined as a catarrhal dermatitis, exudation being evident in its dryest clinical phase. The stimuli responsible for an outbreak of eczema are, even now, little known. They are certainly nervous reflexes in some cases, autointoxicants (gout) in others. Microörganisms complicate the process always when it has been in existence for a short period, but it has never been proved that the primary vesicle of the disease contains bacteria, much less that they have anything to do with the causation of eczema. "Parasitic eczemas," so called, are best relegated to the class of seborrheic dermatitis or else regarded as contaminations.

In spite of its varied clinical forms, the process is always the same. There is first congestion, then edema and exudation in the corium, particularly the papillary layer, the exuded cells at first sheathing the vessels, but spreading later in a uniform

mass throughout. The cells are chiefly lymphocytes and polynuclears. Proliferation of fibroblasts is present in acute outbreaks and is a marked feature in old patches. Eczema exerts its marked effects on the epidermis where intercellular edema, parakeratosis and acanthosis are present in different degrees, their combinations giving rise to the diverse clinical pictures. In acute vesicular eczema, this fluid collects in droplets beneath the horny layer, into which pus-cocci find their way and cause tiny abscesses. In eczema madidans the fluid is poured out in such quantity that the horny layer is washed away completely, leaving a sodden rete from which drops exude to run down or dry on the surface. Eczematous crusts are formed of fibrin, cell detritus and numberless organisms. The last stage of every eczema is desquamative. The scaling is a result of the parakeratosis and the scales themselves are composed of partially cornified cells, in which nuclear remains are often to be seen. Acanthosis is shown in the thickening and lengthening of the interpapillary projections and in increase in depth of the whole epidermis.

*Seborrheic dermatitis* (Unna's *eczema seborrhoicum*) differs histologically not at all from true eczema but its etiology is different. A great deal of painful labor has been expended on this question of causation. It is hard to frame a clear-cut statement which will not mislead. I believe that no one will deny the presence of the morococcus in the earliest lesion. This is a minute, round organism which stains readily with methylene blue, may be cultivated on ordinary media and occurs in colonies, not unlike the appearance of the mulberry from which its name is taken. It has been reinoculated with success, producing characteristic lesions, so Unna says. It is found in the horny layer, the vesicular fluid and lymph spaces. Accompanying it often is the flask bacillus of Malassez which is regarded as a modification of the morococcus, as both may be of the staphylococcus. Many investigators deny any etiological rôle to the morococcus in spite of its constant presence.

Certainly, the disease is both hetero- and auto-inoculable, which eczema is not.

*Psoriasis.*—This disease approaches closely to scaling eczema and seborrheic dermatitis. In fact, there is no dividing line, in either a clinical or a pathological sense. Cell infiltration and fibroblast proliferation are less marked than in eczema of the same degree of acuteness. There is not a great deal of edema present. The histological condition is a dry catarrh, among whose effects parakeratosis is most prominent. The scales are thick and may show only partly keratotic cells throughout or the central portion may be edematous and the outer completely cornified. There is no stratum lucidum and the rete is thinned except for an increase in length of its interpapillary projections. The latter may pursue a tortuous course and may anastomose with neighboring rete pegs. The papillæ, lengthened correspondingly with the epidermic prolongations covered by a thinned rete, reach close to the surface, scale, and their tips are often exposed when the scales are torn off. Nothing is known of the etiology of psoriasis.

*Dermatitis exfoliativa* occurs either as a sequel to other inveterate scaling conditions or in single or recurrent outbreaks as part of a systemic intoxication. The exciting agents include drugs and bacterial toxins, particularly those of pyogenic organisms and the tubercle bacillus. Leucocytosis is very slight as a rule, congestion is marked and edema evident, at least in the early stages. The epidermis is never raised in vesicle formation. The rete is edematous as in psoriasis, the granular and clear layers have disappeared and parakeratosis is less noticeable than in the conditions just discussed. Acanthosis appears, but to no great extent. In the *pityriasis rubra* of Hebra which succeeds repeated attacks of dermatitis exfoliativa, or persistent psoriasis, or arises spontaneously without antecedent scaling, nearly the same conditions are found. The disease invariably ends in death, usually through intercurrent tuberculosis; in its terminal stages, the whole of the epidermis

and corium are thinned by atrophy of their cells and connective tissue. Congestion and fine desquamation remain to the end.

*Pityriasis rosea* is a superficial inflammation of very slight grade. There is congestion of the vessels of the cutis with a slight and irregular leucocytosis; the epidermis is thickened in its horny layer, the intermediate strata between it and the rete having disappeared. No organisms have been found.

*Pityriasis Rubra Pilaris* of Devergie is synonymous with the lichen ruber acuminatus of the Vienna school. Its first sign is a keratosis, an increase in the horny layer about the openings of the lanugo hair-follicles on the backs of the hands and the extensor surfaces generally. The cornification spreads only a short distance down the follicle. In the course of time, inflammatory phenomena appear in the neighborhood of the plugs, the vessels are dilated, a few leucocytes infiltrate and edema brings the usual changes in the epidermis. The disease may finally lead into pityriasis rubra of Hebra, in which case the whole surface becomes red and scaling and the perifollicular keratosis may disappear.

*Lichen Planus.*—The efforts to connect this disease with pityriasis rubra pilaris have failed. Its pathology is its own. In the earliest papule there is an infiltration of cells about the dilated vessels of the papillary layer only. The reticular layer is not affected. The cell infiltration is dense and its character is in dispute. The majority of observers are agreed that it is almost purely lymphocytic, while others assert that the cells are of connective-tissue origin and that the disease is a granuloma. The papillæ and epidermic projections are increased in length and the latter are also widened at the expense of the former. The horny layer is thickened, the rete cells are increased in number and flattened laterally by pressure of the infiltration beneath. In persistent cases hyperkeratosis may become so marked that the papule resembles a wart and is then called lichen corneus. In other instances, in addition to over-

growth of the epidermis, a process of organization goes on in the exudate, new vessels and new connective tissue are formed and the condition is termed lichen hypertrophicus. In involution, the infiltration disappears by degeneration and absorption and deep pigmentation as in syphilis occurs. Masses of granular pigment appear in the dilated vessels and are picked up by the lining endothelium. The granules are then passed on to wandering branched connective tissue cells resembling fibroblasts (chromatophores) and by them deposited finally in the cells of the germinal layer or left lying free in the spaces of the cutis.

*Prurigo* occurs in the tiny papules whose genesis is probably the same as for urticaria; in fact, chronic urticaria is in children likely to become prurigo in the course of time. The papule shows on section a general inflammation of the corium, the cells being chiefly lymphocytic and most abundant about the vessels. Edema is present in sufficient amount to cause a vesicle formation. The serum soon dries however and leaves a thickened epidermis capped by a blood crust, the result of injury. A peculiar feature of prurigo is cell infiltration of the arrectores pilorum, and in older lesions a marked hypertrophy of their bellies. Fibroblast proliferation results finally in increase of the collagenous fibers of the corium.

*Erysipelas* is due to the presence in the cutis of the streptococcus of Fehleisen which is morphologically and culturally identical with the streptococcus pyogenes. It gains entrance through a solution of continuity and may be found in zoögleic masses in the lymph vessels. In the corium the process is an edematous and necrotic one; when it penetrates the subcutaneous tissue, it takes a frankly purulent character and becomes a cellulitis. The cutis presents a peculiar appearance. Its vessels, lymph and blood, are enormously dilated, their endothelium fairly intact and their contents showing a strikingly small number of leucocytes. They do not appear even in the neighborhood of the masses of cocci. The toxins not only

destroy them but seem to exercise a negative cytotactic influence upon them as well. Outside the vessels, there is great edema, the tissue elements are widely separated and undergoing necrosis, the cells and the nuclei taking only acid dyes. Leucocytosis is as little apparent here as within the vessels. The epidermis is edematous and partly necrotic, its horny layer stripped off or raised in a large bulla. Tissue edema may cause partial collapse of dilated vessels.

## Bullous Diseases.

Next to nothing is known of the etiology of this class of the skin's inflammations. A neurotic origin is imputed to them by almost all observers, in the sense that the word is used in urticaria, meaning a vaso-motor instability of the cutaneous vessels. No changes have been demonstrated in the peripheral nerves or in the central system, with the exception of Kaposi's cases of pemphigus vulgaris, in which sclerosis, which may have been entirely independent, was found in the posterior columns of the cord. These remarks do not apply to zòster in which the origin is now clearly understood.

*Pemphigus Vulgaris.*—There is very little congestion and leucocytic invasion of the corium. Serum is poured out of the vessels in a relatively great quantity for the time required in the production of a bulla. Unlike the vesicular conditions, where bleb formation is adventitious, the cover of the lesion is practically the whole epidermis. Remains of the rete pegs are often seen projecting downward into the fluid. In a recent bulla, the fluid shows fibrin filaments with a few leucocytes, among which eosinophiles have by far the largest proportion. An eosinophilia is also found in the blood of a number of the patients. Polynuclear leucocytes appear with a coccic invasion, which is always a possibility, though no part of the disease. *In pemphigus foliaceus,* the bullæ show the same appearance except that they are flaccid and soon rupture, the broken epi-

dermis with dried serum and cells forming a ragged rim about the site of the bulla. In *pemphigus vegetans,* condylomatoid outgrowths appear on the bases of the blebs, as they do in other conditions. Their origin is probably to be found in local conditions of heat, moisture and bacterial activtiy.

*Pemphigus acutus* and *pemphigus neonatorum* together with the bullous eruptions which occur in the neighborhood of foci of bacterial activity might well be called, as they sometimes have been, septic pemphigus. They have no etiological relationship with true pemphigus, but are due to infections with microorganisms. The acute variety owes its origin to a coccus called by the name of its discoverer, Demme, which may be a modification of one of the ordinary pus cocci. Both it and the pemphigus of infants (a streptococcic invasion) appear in epidemics and may terminate in a general systemic infection. The histology of the bulla is the same in all forms.

*Dermatitis herpetiformis* is a multiform disease, occuring not only in bullæ but in erythematous, papular and pustular forms as well. It has been for many years, and is still in certain quarters, confounded with pemphigus without good grounds. Even more stoutly than the latter affection it is held to be of nervous origin, in spite of failure to demonstrate appreciable nerve lesion.

As a rule congestion is more marked in the cutis than in pemphigus, the leucocytosis of the papillary layer is more marked and the eosinophiles appear in greater abundance. The polynuclear leucocytes, lymphocytes and eosinophiles are chiefly found in the form of sheaths about the vessels. Intermingled with them are proliferated fibroblasts and mast cells. In the formation of a bulla the epidermis is lifted from the papillæ in its entirety and the rete prolongations are seen projecting into the fluid below. The contents consist of fibrin threads with a few entangled white cells, chiefly eosinophiles, the proportion of the latter reaching at times as high a figure as 60 per cent. There is almost invariably an eosinophilia of the

blood. Leredde has claimed that the coincident increase in the eosin cells is characteristic of dermatitis herpetiformis. Scars are sometimes left, when the corium is completely denuded, and pigmentation as in lichen planus is always a sequel of the process. In pustular herpetiform dermatitis, the process is much more severe. The whole papillary and the upper reticular layers are packed with cells and there is a relative as well as an actual increase in polynuclear cells. Fibroblasts and mast cells occur in abundance. Cocci are found and, in the purulent condition following their invasion, there may be partial necrosis of papillæ and rete. *Herpes gestationis* is a dermatitis herpetiformis occurring in the course of pregnancy.

*Pompholyx* is a neurotic bullous affection of the palms and soles. In the author's patients, outbreaks have invariably followed shock and nervous depression. The disease has not, as was formerly thought, any relation to the sweat apparatus and in consequence is not related to sudamen or miliaria.

The process is inflammatory. There is the same mild leucocytic invasion about the distended papillary vesels as in pemphigus and dermatitis herpetiformis, great serous exudation with the formation of a bulla which occurs within the prickle-celled layer, not between it and the papillæ. Owing to the thick horny layer of the palms and soles, the fluid does not readily escape and the rete cells are flattened by the pressure. The fluid contains leucocytes (not a great proportion of eosinophiles) and epithelial detritus. Pustulation is a common accident.

*Herpes facialis* and *progenitalis* are neurotic inflammations which should not be confounded with herpes zoster. Their vesicles appear over an inflamed papillary layer, in the substance of the rete, the covering being formed of the whole horny layer. Owing to the sites, they become infected readily and, in such a case, necrosis is followed by a shallow ulceration. Very little scar tissue results from the healing process.

*Zoster* is the one affection in this category whose neurotic basis is thoroughly established. For years, opinion was divided between this theory and a vaso-motor hypothesis. According to Head's investigations which have set all reasonable doubts at rest, the disease is caused by changes in the Gasserian or spinal ganglia; these may be degenerations but are more commonly interstitial hemorrhages. The active agent of their production is unknown, but it is probably an infection, since one attack usually protects for the individual's life. There may be acute neuritis of varying grade in the peripheral nerves themselves; in old people, the outbreak is often followed by an interstitial neuritis whose changes are of course permanent in the nerve and at times in the skin itself.

The vesicle of zoster appears in the substance of the rete, with a sufficiently thick layer of epithelium below to account for the fact that few scars are formed. The vesicular fluid contains fibrin, leucocytes, a few eosinophiles, epithelial cells and in addition a number of minute, round bodies, free or enclosed in epithelial cells. They are homogeneous and have an affinity for acid dyes. Their resemblance to the so-called vaccine bodies is very striking and like them and similar bodies in carcinoma and molluscum contagiosum, they have been classified as protozoa. There is no fact to support such a theory. It is probable that they are merely the product of cell degeneration, hyalin in all likelihood. The upper part of the corium shows distended vessels, invested by leucocytes with a few lymphocytes. In healing, the vesicle dries into a scab, falls off and the horny layer is regenerated. If it becomes infected, ulcerations and scarring may result. Pigmentation is a fairly frequent sequel.

## Pustular Conditions.

*Sycosis* may be of two varieties, Lacterial and trichophytic. Only the former will be dealt with here. Sycosis is chiefly

coccogenic; Mibelli's bacillogenic disease is excessively rare. The lesion is a perifolliculitis but there is an arbitrary regional division in the use of these terms. Sycosis occurs only in the beard and vibrissæ, folliculitis and perifolliculitis on the scalp and the hairy parts of the body. Favoring productive factors are heat and moisture. The infection is from the outside along the shaft of the hair. In a fully developed folliculitis, the hair is loosened from its sheath, partly disintegrated by the invading pus and covered by a mass of cocci, usually white staphylococci. The blood-vessels in the neighborhood of the follicle are distended and packed with red corpuscles. The connective tissue fibers are separated by edema and numbers of leucocytes, closely packed near the hair bag, the infiltration fading away until it becomes only a vascular sheathing at the periphery. A pus cavity is formed at the center which contains the remains of the follicle. The purulent detritus usually finds a vent at the surface, destroying the epidermis, but at times it finds an easier passage to the subcutaneous tissue and collects in abscesses of considerable size. Partial destruction of the follicle entails no loss of hair but when the hair-papilla is lost, no new growth ever appears. Complete baldness results from folliculitis decalvans, a scalp disease, although pus formation is not so marked as in sycosis.

*Furuncle.*—A boil is a staphylococcic infection through the hair-follicle, like sycosis, but the result is very different, probably due largely to feeble resisting powers in the tissues. The process extends laterally and into the hypoderm almost at once. Large abscesses are not formed usually; the cocci find their way from the follicle along the lymph channels and edema and leucocytosis follow their course. Collagenous connective tissue is destroyed and the necrotic mass with leucocytes and bacteria forms the central "core" or slough which appears at the point of entrance and ramifies throughout the inflamed area. After its spontaneous separation or removal, healing by process of granulation takes place. *Carbuncle* is identical in its histo-

pathology with furuncle but of greater extent and presents numerous sloughing areas.

*Ecthyma* is rather a consecutive lesion of the skin than a clinical entity since it occurs in the course of many diseases, notably those attended by pruritus. Through a solution of continuity in the epidermis, staphylococci gain entrance to the cutis, weakened in resisting power; the point of infection is oftenest produced by scratching and is independent of the hair-follicles. The beginning of the condition is seen in a pus collection in the papillary body, serum and leucocytes percolating into the epidermis. The abscess may be quite large and may raise the horny layer in the form of a pustule. After a time, the pus and epithelium dry into a thick crust which rests on the cutis, the surrounding skin intensely inflamed. The loss of tissue is always superficial and yet deep enough to heal only with scar formation.

*Impetigo Contagiosa* has been divided by Sabouraud into two varieties, those of Bockhardt and of Tilbury Fox, the first perifollicular and due to the streptococcus, the other not so situated and caused by the staphylococcus. The distinction is too fine for use. Location is probably altogether accidental and the staphylococcus albus and aureus the chief offenders. Unna says they have peculiar cultural characters in this condition and doubtless they have, for the infection is always mild. The streptococcus may be causative in the beginning of certain lesions and disappear before other pus-cocci later. In any case we are dealing with a superficial pustulation in the epidermis. The horny layer is lifted at the outset by a fluid collection which at this time contains few leucocytes. Later it becomes frankly purulent and dries with the covering epidermis to a crust, which is stuck on, not set in the skin as in ecthyma. The base of the pustules is formed by a larger part of the rete and on subsidence of inflammation the stratum corneum is reformed without scar or pigmentation.

*Acne* is an inflammation about the sebaceous glands. In its site of predilection, the central portion of the face, the lanugo hairs are appendages of these structures, reversing the condition in sycosis in which the follicle is primarily involved. The basis of the acne pustule is the *comedo* which is not formed of inspissated sebum as was long held but of concentric layers of horny material. In other words, at the time of puberty when circulatory changes occur about all the skin appendages, one of the effects is a hyperkeratosis of the sebaceous opening. The outlet blocked, sebum collects behind the comedo and the gland is distended. A certain amount of the fatty matter penetrates the horny plug together with multitudes of bacteria. Sabouraud states that his "microbacillus of seborrhea" is the chief factor in comedo formation but the investigations of others have not supported his contention. The pus organisms are white and golden staphylococci and the streptococcus. Remaining quiescent for a time, they finally cause congestion in the periglandular plexus, followed by a leucocytic invasion. When the latter is of light grade, inflammation may resolve without destruction of the gland, but a small abscess is usually formed which causes destruction of the appendage and finally points about the opening. This is called acne vulgaris. In the worst cases, especially when the skin is thickened as the result of previous inflammation, instead of breaking through the skin, the pus burrows beneath it, and several lesions coalesce into subcutaneous abscesses. The process is then called acne indurata.

*Acne varioliformis* occurs about the border of the scalp anteriorly, is a necrotic perifolliculitis, a central slough separating with the hair as in furuncle and leaving a depressed scar much like the pits of variola.

*Dermatitis papillaris capillitii* (acne keloid) occurs on the neck at the edge of the scalp, in persons, negroes especially, in whom a keloidal tendency is marked. The beginning lesion is a pustular perifolliculitis, which is followed by a formation of

new connective tissue in thick bands parallel to the surface. Coincidentally, there is a dilatation of the vascular channels into large angiomatoid spaces, which may result from obstruction of outflow by the new keloidal growth.

*Rosacea.*—This process has nothing to do with acne; the name acne rosacea is a misnomer. It is divided into three stages, hyperemia, pustulation and hypertrophy. The first evidence of the disease is a dilatation and lengthening, causing tortuosity of the superficial vessels. There is slight edema of the tissues and evidence of subacute inflammation in the shape of an emigration, chiefly of lymphocytes. Later, pyococci gain entrance through follicles or sebaceous glands and small abscesses are formed, infiltration becoming leucocytic. The abscesses may be independent of all the appendages. In the third stage, the long-standing edema stimulates the activity of all the cells, fibroblasts and epithelium. The sebaceous structures are greatly hypertrophied and surrounded by dilated vessels and new collagenous fibers. Pustules dot the surface here and there and the whole cutis is infiltrated by polynuclear leucocytes and lymphocytes, with fibroblasts showing occasional mitosis and a few mast cells.

*Hydradenitis Suppurativa.*—It is likely that hydradenitis is the same process as the one called acne varioliformis and various others to which no less than eleven appellations have been given. The author prefers to call it necrotic granuloma as indicating its nature and committing the description to no particular appendage. The precedent conditions are a persistent acroasphyxia and often, though not always, systemic diseases, among which tuberculosis is easily first. The inflammatory process begins deep in the reticular layer and subcutaneous tissue, about the plexuses of the sweat coil (hydradenitis), follicle (acne) or independent of them both. It is almost impossible to suppose an external infection for such a condition. The nodules are at first composed chiefly of lymphocytes and plasma cells with a few leucocytes; later, epithelioid and giant

cells appear and the nodule undergoes a central necrosis which, if not coagulation necrosis, is nearly allied to it. Neighboring foci coalesce until, by extension, the epidermis is involved and exfoliates; the necrotic mass is separated. As there is loss of substance, there is always minute scarring as a sequel.

## Atrophies.

*Alopecia Areata* which has no relationship with any other of the many forms of baldness is really an inflammation of light grade, but as its chief symptom, pathological as well as clinical, in loss of hair, it is best considered here. Sabouraud claims that it is due to the same microbacillus which he regards as the causative agent of seborrhea and acne, as well, but, as in acne, he has found no supporters in alopecia areata. Microörganisms are present in numbers early in the disease, but, according to Robinson and Walker, they are the staphylococci epidermidis albi of Welch, slightly modified in cultural characters. An areate alopecia has been produced by it in rabbits. There is very little inflammation present about the follicles. Interference with hair growth seems to be caused by toxin acting on the hair-papilla. The hair is at first thinned, then expands again so as to produce the characteristic exclamation point appearance ( ! ). When the dot is formed, the hair is lost, leaving the follicle empty. After a time, new growth begins in the form of a white, lanugo, tapering hair, the lack of color due as always to loss of medullary pigment, not presence of air in the shaft. Later, hairs appear of the normal size and color. In total alopecia, after the formation of a few lanugos, the papillæ may atrophy, the hair bag disappear and baldness is permanent.

*Scleroderma.*—There are two forms of the disease, a localized (morphea) and a generalized one which belongs to the domain of neuropathology. Localized scleroderma begins in the form of a vascular dilatation accompanied as in keloid by

a perivascular proliferation of fibroblasts. These fibroblasts produce new collagenous fibers which appear in thick bands and in turn cause an obliteration of the blood-veessels by pressure. Finally, the blood-channels appear as hyalin threads and failure of nutrition produces an atrophy of all the cutaneous structures, the terminal stage of the disease.

## Hypertrophies.

Increase in the thickness of the horny layer or interference with its proper formation produces various lesions which may be classed as *keratomas*. Among them are cutaneous horns, corns, callosities, seed warts, keratosis pilaris, a relative of ichthyosis (*vide infra*) and other conditions difficult to classify. The dividing line between tumors, hypertrophies and inflammations is a very narrow one.

*Condyloma acuminatum* results from an overgrowth of the entire epidermis, evidenced by increased thickness of horny layer and rete, and mitotic figures in the germinal cells. As a result, the epithelium is thrown into projections, into the concavities of which the papillary vessels and connective tissues follow. The vessels are enlarged but contrary to what might be expected, there is little or no evidence of fibroblastic proliferation. This papillary formation is rarely simple, offshoots appear on the parent stem, giving finally a cauliflower appearance. Condylomata acuminata appear in favoring conditions of warmth, moisture and uncleanliness (bacterial invasion?) notably about the genitals.

*Molluscum contagiosum,* if not actually a contagious affection, is certain auto-inoculable. In spite of many efforts, no organism has ever been recovered from its tumors. The rete is the portion chiefly affected. The horny layer is lost in a fully developed lesion and an opening leads down to the center of the mass, which partly projects above the surface and partly into the corium. Its lower border bounded by connective tissue is often lobulated in the fashion of sebaceous glands. The

germinal cells are reduced in height and the neighboring rete cells have largely lost their prickles. The characteristic feature of molluscum contagiosum is a degenerative process which appears in the mucous layer. Small areas of degeneration appear in the cells, which take eosin readily and are possibly composed of hyalin material. They increase in size and coalesce until the whole cell body is occupied. These are the "molluscum bodies," so called, which like all similar degenerations have been held to be protozoa. They lie free in the central cavity and may be extruded by pressure as a milky fluid. (Pt. I., p. 259.)

*Ichthyosis.*—There can hardly be any question that ichthyosis is a congenital deformity of the horny layer. Unna, in one of his vagaries, classes it among infectious inflammations. The fact that it is rarely seen before the end of the first year is readily explained by the tendency of infants' skins to exudation under slight irritation which the process itself supplies. Bowen's theory is the most tenable yet presented — that it is the result of the persistence of the fetal epitrichial layer of balloon cells. Histologically, the chief change is an increase in thickness of the horny layer with a marked thinning of the rete. Although the secretions are noticeably lessened, there is no perceptible change in the number, size or appearance of the sweat and sebaceous glands. The papillæ are elongated and taper to a point. Ichthyotic skin is susceptible to all forms of irritation; the type of the resulting inflammation is eczematous. Consequently, there is usually present in the corium a greater or less degree of subacute, catarrhal inflammation, evidenced by the presence of lymphocytes, leucocytes and fibroblasts. This mild grade of ichthyosis is called xeroderma; ichthyosis hystrix shows thick plates and spines of horny material not unlike the ectoskeleton of the saurians. The keratotic layer is apt, like the tip of the comedo, to become blackened in time, either from dirt ground in or a change in the character of the keratin.

*Pigment Hypertrophies* appear spontaneously, independently of inflammation or new growth, in the shape of freckles( lentigo) or moth-spots (chloasma). The change is the same in both, an increase of a non-ferruginous pigment contained in the germinal layer and in chromatophores wandering through the corium.

*Elephantiasis* occurs in two forms, the Arabic and the Greek as they have long been called. Both result from obstruction of the lymphatic circulation, but the blocking is due to different causes. In elephantiasis Arabum, it is caused by the presence in the lymph radicles of the ova of the filaria sanguinis; in elephantiasis Græcorum by a variety of scar-producing conditions, syphilis, tuberculosis, surgical operations, etc. When the obstruction is set up, the lymph vessels dilate and a portion of the fluid is exuded into the surrounding tissue where it stimulates the fibroblasts to proliferation and formation of new connective tissue. In the process of contracture, the new fibers press upon lymphatics and veins and fresh ones are occluded. The vicious circle thus set up causes ultimately an enormous increase in the size of limbs, scrotum or vulva as the case may be. The epidermis is thickened, verrucous in places, and deeply folded. Here and there the epithelial layer becomes thinned from the pressure of a lymphangiectasis below and finally ulcerates, permitting the escape of a milky fluid. (Pt. I., p. 249.)

## Hemorrhages.

*Purpura* is symptomatic of many diseases and injuries of the skin. It is evidenced histologically by the pressure of red corpuscles or hemoglobin granules in the lymphatics and between the fibers of the corium. Inflammation may or may not be present. The term is not applied to bullous or vesicular lesions which have become hemorrhagic. Purpura occurs after direct violence and from bites of insects such as the body

louse, in the course of almost all inflammations, exceptionally, such as syphilis and variola, in scurvy (purpura hemorrhagica) and with or without erythema as purpura rheumatica. The last is generally the result of a pyococcic infection, is accompanied by inflammatory changes, and in severe cases there may be localized necrosis followed by ulceration. Extravasation of blood is due to one of two causes in the skin as elsewhere, the presence of a hemolytic ferment or weakness of the capillary walls. In *purpura senilis,* where hemorrhage occurs spontaneously, Unna has demonstrated changes in the endothelial lining with thrombosis and rupture of the capillaries.

## Granulomas.[1]

*Syphilis.—Chancre,* the initial lesion of syphilis, results beyond question from the entrance through a break in skin or mucous membrane of a microörganism which has hitherto eluded all research. The claims of Lustgarten, Van Nieson and others of the discovery of a bacillus have never been substantiated. The first change is great congestion, followed by an exudation composed almost entirely of plasma cells (see introduction to this chapter) and lymphocytes. They first appear closely packed in sheaths about the small vessels, so far as can be judged from the advancing border. The lesion is always necessarily far advanced when excised for examination. The pressure which the plasma cells exert upon each other causes them to assume a polyhedral shape, as also the few epithelioid cells dotted throughout the exudation. The connective tissue, collagen and elastin, largely disappears but threads may be traced traversing the cell mass. At the periphery, the rete prolongations are increased in size but over the center they have disappeared as a result of pressure, the rete is thinned and the horny layer often exfoliated. The vessels of the corium show changes of various grades, from a mere swelling of endothelial cells to a panarteritis with proliferation of

[1] See also Pt. I., pp. 251-257.

the lining sufficient to occlude the lumen. Remains of the capillaries can be seen forming the center of almost every focus of emigrated cells. It is possible that outside pressure has also something to do with capillary obliteration. The immediate neighborhood of the vessel, deprived of its nutriment, undergoes necrosis. Under a lower power, the field can be seen dotted with the pale foci of degeneration, if only a basic stain is used (polychrome methylene blue). In addition to the cells described, a few mast cells may be found at the edge of this infiltration and in exceptional cases, here and there, a Langhans giant cell with protoplasmic filaments extending into the surrounding tissue. Chancre is not in itself an ulcerative process; when ulceration occurs it is from a superadded infection from pus-cocci or the bacillus of chanchroid. Necrosis begins beneath the epithelium, spreading to it and the tissue below. Numbers of polynuclear leucocytes appear near it. After a time the necrotic material separates and an ulcer with sharp edges is left. The extreme hardness of chancre is due solely to the density of its infiltration. When the process of repair begins, the cellular elements undergo fatty degeneration and are absorbed, leaving numbers of fibroblasts, which produce an amount of collagenous material totally incommensurate with the needs of the occasion. This constitutes the usually permanent scar of chancre.

*Papular Syphiloderm.*—As the papule forms the basis of all early lesions of syphilis, one description of it will suffice. Ulceration and pustulation do not alter its character sufficiently to prevent its recognition. It is well to remark that in the absence of tubercle bacilli, differentiation is impossible between it and disseminate tuberculosis. The papule begins like chancre in the form of an exudation of plasma cells and lymphocytes about the dilated, congested vessels of the cutis and hypoderm. With the exudation, there is a proliferation of adventitial fixed cells which appear chiefly in the epithelioid form. A small number of mast cells are to be found at the periphery. As the

lesion grows older giant cells are formed here and there. The vessels show endothelial proliferation which obliterates them at times and causes focal necroses. The epidermis is flattened and thinned over the densest part of the infiltration, its rete pegs increased in size at the periphery. Resolution is the same as in chancre with a resultant pigmentation whose mechanism does not differ from that described under lichen planus.

*Chancroid* has at last been established as a definite disease by the cultivation and inoculation of its bacillus. The organism is short (streptobacillus of Unna), occurs in chains in the tissues and irregularly in the necrotic detritus. It was discovered by Ducrey and cultivated on serum-agar first in 1896 by Lenglet, whose work has been confirmed. It is recovered with great difficulty from the pus either of the sore or the bubo. There are many ulcerations about the genitals due to pus infection which are not chancroids. The bacillus gains entrance through broken epidermis to the papillary layer where it forms a small abscess, the course through the epidermis marked by leucocytes surrounding bacillary chains. They are never seen in the protoplasm of phagocytes. Outside the abscess is a zone of plasma cells, not so densely packed as in chancre, from which lines of emigrated cells radiate, following the course of the congested vessels into the hypoderm. At the edge of the plasmoma a few fibroblasts and mast cells are found. The epithelium is edematous and infiltrated with pus. Necrosis begins early and superficially, destroying the epidermis and corium beneath so that the edges overhang. In a fully formed chancroid, the surface is covered with débris containing many leucocytes and bacteria bounded by successive zones of necrosis with bacilli and fragmented nuclei, the plasmoma much reduced in thickness and peripherally congested. Leucocytes migrate through the whole diseased area. The floor is uneven, due to the fact that tissue death occurs first in the neighborhood of the chains radiating from the ulcer into the edge of the plasmoma. Bacterial activity is finally overcome by the leucocytes, probably,

since their number constantly increases, and, after sloughing or absorption of necrosed tissue, healing takes place by scar formation.

*Tuberculosis.—Tuberculosis verrucosa cutis* is the commonest form in this country and is due to a direct inoculation, generally of the hands, with Koch's bacillus which is usually found with comparative ease. The whole cutis and hypoderm is the seat of a diffuse tuberculosis. The chief cellular elements are plasma cells, lymphocytes, epithelioid and giant cells, the last derived from fibroblasts whose protoplasm has not kept pace with nuclear division and usually containing the few bacilli to be found. There is no regular arrangement of the cells into typical tubercles. Threads of connective tissue run irregularly through the mass. Necrosis is uncommon. At the base of the elongated projections are found numerous miliary abscesses. They may be caused by pyococcic contamination but the organisms are difficult to find. There is a great degree of acanthosis, the rete pegs are elongated, sometimes club-shaped or digitate at the extremity, the lower border perhaps lost in an abscess. The horny layer is enormously thickened by hyperkeratosis and raised into the verrucous formation which gives the disease its name.

*Lupus Vulgaris* is a tuberculosis of lower grade and slower growth. Bacilli are demonstrated with difficulty by scraping the tissue and smearing it on a slide. The lesion of lupus is the "apple-jelly" nodule which is always to be found. It consists of small cellular areas in the cutis and hypoderm, composed chiefly of plasma cells and lymphocytes, with a few productive elements, epithelioid and giant cells, the latter noticeably less than in tuberculosis verrucosa. Between the cells and running generally perpendicular to the surface is a network of fine fibers, the lupus reticulum, which is composed chiefly of elastic fibers, because of their great resistance. The giant cells contain the bacilli which average about one in 200 sections examined. Epithelium remains intact, slightly acanthotic. This

is the simplest form of the disease. As in tuberculosis of the lungs, adventitious elements change its complexion somewhat. There is a catarrhal lupus in which coccic infection causes a masking of the lupoma by leucocytes, with a thinning or loss of epithelium, crust formation and ulceration (lupus exulcerans). In fibroid lupus, the toxin causes proliferation of fibroblasts with formation of new connective tissue. Giant cells are more numerous and other elements fewer in this type. Acanthosis is marked and forms the basis of the malignant epithelioma which sometimes complicates the disease. Lupus verrucosus shows a hyperkeratosis over the lupoma. Necrosis is no part of the process *per se*. Direct inoculation is rare in causation.

*Scrofuloderma* and *Scrofulous Gumma* are tuberculoses of the hypoderm, infection being carried to it by lymphatics from subjacent nodes or bone. Tubercle bacilli are not easily demonstrated except by inoculation into animals. The disease is almost a pure exudation of lymphocytes and plasma cells about lymphatic vessels; productive elements are excessively rare. Infiltrated areas undergo early a liquefactive necrosis and small, sterile cold abscesses are formed. If unchecked, the disease extends to the surface and breaks through, leaving indolent ulceration with fistulous tracts to the original focus. Thrombosis is not a feature of this type of tuberculosis.

*Tuberculosis Vera* (orificialis, miliaris) occurs about the mucous outlets from inoculation of bacilli in visceral discharges. It is superficial, the only cutaneous disease showing formation of true tubercle, ulcerates readily and contains myriads of organisms.

*Lichen Scrofulosorum* is a perifollicular disease, occurring always in the tuberculous, in which it is almost impossible to demonstrate bacilli. Inoculation fails in a great majority of instances. Either the toxins alone are at work here or the process once started continues after the bacilli have disappeared. Color is lent to the former theory by the fact that

injections of tuberculin have caused outbreaks. Histologically, lichen scrofulosorum is a productive tuberculosis with little tendency to necrosis.

*Erythema Induratum Scrofulosorum* is unquestionably a tuberculosis of the hypoderm, the same remarks as to finding bacilli being applicable here as in the lichen of the scrofulous. Inoculation has been successful in only two or three cases. While examination shows an exudative condition generally, productive elements may occur in large proportion. Lymphatics are chiefly involved and cold abscesses are formed as in scrofuloderma, from which erythema induratum is differentiated by a pronounced thrombotic tendency in the smaller vessels. The infiltration extends to the skin and causes ulceration at times.

*Leprosy* is seen in three forms, the nodular, anesthetic and mixed. All are produced by Hansen's bacillus which resembles that of tuberculosis in almost every particular, and which gains entrance, according to his and Morrow's observations, by the nasal passages. The *nodules* of leprosy resemble a productive tuberculosis; lymphocytes and plasma cells are few, the bulk of the lesion being made up of vacuolated and multinucleated cells (lepra cells). Bacilli are found in them and free in the tissues in great numbers. In *anesthetic* patches, bacilli are much fewer, infiltration is slight and the chief changes are found in the sensory nerves, especialy the cutaneous filaments showing marked degeneration. The bacilli are easily seen in the peri- and endoneurium. Their first effect is to cause a parenchymatous neuritis which in its later stages becomes also interstitial and involves motor nerves as well. Mixed leprosy combines both forms. There are no changes in the central nervous system.

*Rhinoscleroma* is a granuloma affecting the nasal and throat mucous membranes and adjacent skin. It is caused by an encapsulated organism which is easily found and conforms entirely to the characters of Friedländer's pneumococcus. The disease shows the usual features of granuloma, lymphocytes,

plasma, epithelioid and a very few giant cells without regular arrangement and traversed by threads of fine connective tissues forming a reticulum. Necrosis rarely occurs.

*Blastomycosis* is primarily a skin affection, from whose foci systemic infection may take place. Its organism is a yeast fungus, the blastomyces described by Busse and Gilchrist independently, a double-contoured round body about 10 $\mu$ in diameter, which stains readily with methylene blue and can be cultivated on almost any medium. Outside the body, it forms a mycelium, inside it increases by budding as do the yeast fungi generally. The cutaneous lesion is singularly like that of tuberculosis verrucosa, clinically and pathologically, except that it ulcerates rather readily. The cutis and hypoderm are invaded by the same productive granulomatous process, there is an overgrowth of the epithelium, both acanthosis and hyperkeratosis with abscesses at the tips of the elongated rete pegs. Blastomycetes are found free, in the abscesses and in the substance of giant cells.

*Granuloma Fungoides* (*Mycosis Fungoides* of Alibert.).—In spite of its multiform clinical characters, granuloma fungoides shows the same pathological picture from beginning to end. It has certain remote relationship to sarcoma but it never forms metastases in nodes or viscera. The finding by McVail of a white bacillus has not been confirmed. Bacteria have been recovered often but are regarded as contaminations.

The process begins in the papillary body, and confines itself strictly to the upper part of the corium. There is congestion and exudation of small numbers of white corpuscles, mononuclear predominating, but the mass of the cells is made up of bizarre forms derived from fibroblasts. Some are small, polyhedral from pressure with acidophile protoplasm and a vesicular nucleus, others are larger and distinctly epithelioid and giant cells partly or fully formed appear scattered irregularly, the whole traversed by a fibrous reticulum. The giant

forms are not numerous. The epithelium shows catarrhal changes with scale formation, rarely crusts. When the cell mass becomes large, its central and superficial portion dies, possibly as a result of pressure on the vessels. Necrosis is followed by absorption or exfoliation of epidermis and ulceration. Large tumors occasionally undergo complete absorption, leaving the corium weakened in resisting power. The epithelium at times assumes a proliferative action which microscopically cannot be distinguished from squamous-celled epithelioma. Granuloma fungoides invariably results in death from cachexia, if not from intercurrent disease.

*Xanthoma* is a name applied to several yellow tumors only one of which properly belongs here. *Xanthoma palpebrarum* is caused by a fatty degeneration of the muscles of the eyelids, its only situation. *Xanthoma tuberosum* or *vulgare* is a near relative of lipoma according to Török, a development of fat in a heterotopic situation, the corium. The cells in which the fat droplets are contained are large mono- or multinucleated cells ("xanthoma cells") undoubtedly of connective tissue origin. Inflammation is not present except under irritation. Tuberose xanthoma is sometimes accompanied by jaundice, which is thought to be obstructive since the tumors have been found in the bile-ducts. *Xanthoma diabeticorum* is a granuloma possibly due to a toxemia occurring in diabetes and in its allied state, obesity. It first appears as a subacute inflammation about the vessels of the reticular, the exudation composed of lymphocytes and fewer plasma cells. An added element soon appears in the shape of mast and epithelioid cells. The endothelium of the capillaries is swollen and in its cells, or in the epithelioid, fatty degeneration occurs. The fat breaks through the cell wall and escapes into the surrounding tissue where it lies in tiny droplets or collects in larger masses. In alcohol specimens where the fat is dissolved, empty spaces are seen traversed by protoplasmic filaments, remains of degenerated cells. The only connection between the three forms is

the presence of fat in the cutis which gives the characteristic yellow color.

*Lupus Erythematosus.*—The disease is an inflammation with an ultimate necrosis and death. Its relationship to the granulomas is problematical; its connection with tuberculosis cutis even more so. Great efforts have been made in latter years to prove its tuberculous origin, a theory which is particularly strong in France. Many cases do occur (more than a majority) among the tuberculous. No organism has ever been recovered from the tissues.

Erythema, which means congestion and exudation, is the first change, always about the superficial vessels. There is a fair amount of edema followed by the usual epidermic phenomena. Acanthosis results, with scale formation and keratotic prolongations into the openings of the pilo-sebaceous follicles. Except in the earliest stage when it appears about the vessels, there is no regular arrangement of the cellular infiltration. It is confined to the papillary body and upper part of the reticular layer and consists of lymphocytes, plasma cells, very few leucocytes, and fibroblastic derivatives chiefly of the epithelioid type. Capillary thrombosis occurs simultaneously with the attainment of the height of the infiltration. The walls of the vessels appear to be intact but the clot blocks them completely. Lack of nutrition causes a degeneration not unlike coagulation necrosis in which not only the infiltration but the skin appendages disappear. The thinned epidermis is left covering an atrophic depressed area from which the detritus has been asborbed. Capillary obstruction brings about a permanent dilation of the vessel near the thrombosed area.

## Parasitic Diseases.

**Animal Parasites.**—Description of these parasites is properly confined to works on zoölogy. Their number includes those which live on the skin like the *pediculus capitis, corporis*

and *pubis,* varieties of the same species and those which pursue at least part of their lives in its substance like the *acarus of scabies,* the female burrowing in the epidermis and leaving in the furrow a trail of ova and feces, or the *demodex folliculorum,* a segmented worm which has its habitat in the sebaceous glands and sometimes causes a brown pigmentation. All are capable of causing irritative inflammation.

**Vegetable Parasites** include the ringworm fungi, the achorion of favus and the fungi of pityriasis versicolor and erythrasma.

*Ringworm Fungi.*—There are several varieties of the fungus, chief of which are the large- and small-spored. Both are concerned in the production of ringworm of the beard. Differentiation lies not so much in the size of the spores as in their arrangement. The small species sheaths the hairs, is rarely seen in mycelial threads and being closely packed appears in the form of a mosaic. The large-spored fungus occurs outside and inside the hair (ectothrix and endothrix) in chains, "rosary" arrangement. They can be demonstrated as can all fungi by placing the hairs or scales in a dilute solution of caustic potash. They may be stained in a solution of gentian violet in aniline water, decolorizing by Gram's method. Both may cause intense exudative inflammation. Cultural characters differ in some particulars. (Pt. I., pp. 210-213.)

# CHAPTER XXIII.

## DEATHS BY VIOLENCE AND POISON.

### Lesions in Asphyxia.

The blood is dark and usually fluid, the hypostatic congestion is dark, face cyanotic, organs in condition of passive hyperemia. Respiratory mucous membrane in parts or generally injected and bronchi contain frothy, blood-stained mucus, especially if the fatal process was slow. The lungs contain more dark blood if process rapid, with subpleural and subpericardial bleeding; partial emphysema is common. Right side of heart and great veins distended with blood, left side may be empty, but if heart action lasted longer than respiration this may not be so. Hanging and choking cause pressure on the carotids, jugulars and vagi; the vessels may be firmly occluded. If the body was immediately cut down there may be no line on the neck made by the cord or rope, otherwise it may be well marked. After hanging the line is evident on the sides of the neck and is lost near the ears; if something was tied around the neck its course is usually horizontal. The skin may show abrasions which turn dry and semi-transparent after death; extravasation may be microscopic. When the death followed choking by the hand, impressions of the fingers and nails, ecchymosis under the skin or in the tissues, fracture of the larynx — rarely of the hyoid — may be found. In both hanging and strangling partial erection of the penis, escape of semen (into the urethra), urine or feces may occur.

Drowning produces the same general conditions, the nails and hands may contain sand, mud or weeds; similar matter may be found in the stomach; the fluid may have entered the respiratory passages. Microscopical examination of such fluid and of the water in which the death occurred may give valuable evidence in medico-legal cases. The lungs may be distended so as to cover the heart and overlap. In recent cases the extensor surfaces of the limbs may show marked cutis anserina, and the scrotum may be shrunken. In recently born infants the presence of a dried umbilical cord, still attached, may be of importance; the back of the tongue and the opening of the larynx may show finger-nail wounds. Foreign bodies in the air passages are usually firm material, portions of food, bits of cloth, etc., introduced by accident or design, the latter often in infants. Vomited matters from the esophagus may also close the larynx or trachea, as during coma from alcoholism. In the new-born cessation of placental circulation during parturition may excite premature efforts at respiration; the subserous hemorrhages in heart and lung are commonly present, and, as in the above cases, froth and foreign material occur in the bronchi.

Other appearances occasionally seen in death from asphyxia are protrusion of the tongue, injected conjunctivæ, ecchymoses on the face, neck and chest.

The distinction should be made between *suffocation,* prevention of air entering the lungs by pressure on the air passages or cloths and other matters held over the nose and mouth, *strangulation,* which means constriction of the neck by cord-like materials, and *asphyxia,* which is the condition of the respiration produced thus and also by irrespirable gases. It is always possible that a death by other violence or poison may be concealed by hanging the body or throwing it into the water; interpretation of post-mortem conditions should therefore be cautious.

*Burning* causes death by involving a large extent of surface or by secondary conditions following this. The inhalation of smoke, hot air and flame, incautious ingestion of hot fluids, and inhaling steam may also be fatal. The greater part of the surface may be destroyed, and if by flame the superficial hairs are crisped, swollen at the ends, or lost; in scalds they may be preserved for a time. The greater part of a limb may be completely charred, or the whole body. The skin is dry, red and hard in less severe cases, or suppurating; in the mildest forms redness and vesicles are formed. The blood cells may be destroyed, with hemoglobinemia.

Congestion and edema of the respiratory passages, often croupous, and of the cranial and abdominal viscera, serous inflammations (pleura and peritoneum), and perforating ulcer of the duodenum with general catarrhal gastro-enteritis, may all be found if the patient survives the first shock of injury.

*Electricity*, either from currents or lightning, may cause superficial burns, and with the latter there are branched markings on the skin, edema and laceration, injury to important viscera, and occasional fractures of bones. There are no characteristic and constant lesions in these cases.

Other deaths by violence show the wound or injury to important viscera (brain), fractures, etc.

## Poisons.

**Alkalies.**—The commonest alkalies causing death by accident or suicide are ammonia, potash and soda. Parts which have been in contact with the chemical are usually swollen and softened, congested and inflamed; black from changes in the blood and peeled off in later stages. These effects are commonly found about the mouth, pharynx, esophagus and stomach. With a stomach full of food the poisonous fluid may ride over to the pylorus and enter the duodenum, while most of the stomach escapes. Inhalation of ammonia causes intense

congestion of the respiratory mucous membrane. Death may follow in a few hours or weeks; recovery may occur with contracting scars in parts attacked.

**Acids: Mineral.**—*Hydrochloric.*—Whitish eschars on parts in contact with acid, false membranes may form; later sloughing and inflammation. Death may occur in a few hours; if later than twenty-four hours, fatty degeneration of kidneys and suppurative inflammation along track of acid may develop. Blood may be fluid or thickened.

*Nitric.*—Yellow eschars (xanthoprotein) in mouth, esophagus and stomach, intense hyperemia and inflammatory reaction, stomach contains a mixture of blood and necrotic tissue, yellow or greenish; it may be perforated.

*Sulphuric.*—Eschars gray or black, mucosa of esophagus black and peels off in shreds, stomach contains black, sticky material, its walls congested and hemorrhagic, rugæ marked and partly destroyed, perforation may occur.

All these poisons depend for their effect upon their concentration and the time during which they act. By accidental entrance to the air passages they produce similar destruction. Their effects often skip a part of the tract from mouth to intestine, being manifest at times only in the lower esophagus, stomach and duodenum. They may retard putrefaction in the rest of the body.

**Acids: Organic.**—*Acetic, oxalic* and *tartaric acids* may cause death, the second most commonly. They may be rapidly fatal or excite inflammation, ending fatally or with scar formation and recovery. The mucous membranes attacked may be hyperemic and inflamed, with oxalic acid commonly white and shrunken, easily stripped off. In the stomach disorganized blood, mucus and necrotic tissue, swelling, opacity and softening of the mucosa, inflammation and gangrene may occur.

*Carbolic.*—The parts attacked are whitened and condensed, there are hemorrhages along the track of the poison, the rugæ of the stomach and the intestinal folds (*valvulae conniventes*)

are thickened and have a peculiar worm-like feel through the unopened organs. The color of the serous surface opposite the action of the acid varies from pink to brick-red, and neighboring organs may show patches of the same tint. The urine may be dark green and its odor, like that of the stomach, is characteristic of the acid. Other organs are usually congested. Death may occur instantly from nervous shock, or later from destructive chemical effects. If the stomach contained food (especially with alcoholic beverages) it may escape the action.

*Hydrocyanic.*—Death may be immediate and only venous congestion, fluid blood, pinkness in the stomach and gut, and the odor of the drug (fruit-like) give evidence of the nature of the case. With potassium cyanide corrosive action occurs, as with alkalies.

**Metallic Poisons.**—*Antimony, Usually as Tartar Emetic.*—In acute cases gastro-enteritis occurs, sometimes peritonitis. In chronic cases there may be no marked lesions.

*Arsenic.*—Inflammation of the stomach, the presence of green particles (Paris green) about the mouth and in the stomach, or white grains of arsenous acid, extravasation of blood, enteritis, swelling of the lymphoid tissues in the canal, peritonitis, nephritis and cystitis may occur. Fatty degerations in viscera are common. The body may be preserved by the poison.

*Copper.*—Inflammation of the gastro-intestinal tract, ulceration and necrosis of its mucosa, perforation and peritonitis are the usual results. A green color may be noticed in the parts.

*Lead.*—The metallic salt in substance (often acetate) may be found in the inflamed stomach and intestines. In chronic cases degenerations of muscular and nervous tissue and chronic inflammation of meninges may be added to intestinal lesions. Nephritis and gout may be associated with these.

*Mercury.*—The bichloride is the common salt used. The mucosa of parts affected is swollen, whitened, hyperemic; later ulceration may occur. Nephritis is usual if life is prolonged.

Severe necrotic inflammation of the colon (diphtheritic colitis) is observed in chronic cases.

*Phosphorus.*—Acute cases present hemorrhage and inflammation in the stomach, the poison in substance (match heads) and a peculiar odor. Vomit, contents of alimentary canal, and feces may glow in the dark. After a few days icterus, subserous and submucous hemorrhages, fatty degeneration of the liver and other viscera, with bile staining, are commonly developed. The liver is particularly affected and may resemble the liver of acute yellow atrophy.

*Carbonic Oxide.*—The characteristic effect of this poison is the cherry-red color of the blood, hypostatic congestion of the surface being also of this color. In some cases there is cerebral hemorrhage from a small branch of the middle cerebral artery. The spectrum of the blood and the corroborative tests should be used to determine the presence of CO Hb. (See p. 370.)

*Sulphuretted Hydrogen.*—Poisoning occurs from working in sewers and privy vaults where the gas collects, and in rare cases from large production in the intestines; the gas may be discovered in the urine. The viscera smell of the gas, the blood is fluid and black, like ink, and vascular organs (lungs) may also be dark colored. This color seen through the skin gives the surface a green or blue-green tint. Rigor mortis may be absent, the viscera are usually hyperemic.

**Alkaloids** of various kinds may cause death, but their presence requires careful chemical analysis of stomach and intestinal contents. If the crude form of the drug is used microscopic examination of the contents of the stomach and intes-tinal contents. If the crude form of the drug is used microscopic examination of the contents of the stomach and intes-tines, and of the feces, may reveal leaves, roots and seeds, or their fragments; these may be sufficiently characteristic to identify the poison.

## Appendix to Chap. XXIII. Synopsis of Lesions After Certain Infections.

**Anthrax.**—Malignant pustule on the surface or diffuse anthrax edema, rigor mortis marked, blood dark cherry red, not much coagulated, diffuse or circumscribed hemorrhages in cerebral membranes, at times small foci of bleeding in brain, catarrhal inflammation of alimentary tract, blood-stained fluid in body cavities and hemorrhages in serous membranes, spleen moderately or much swollen, soft and of very dark red. If infection took place through the alimentary mucosa, edema, hemorrhage in tissues and pustules may occur in pharynx or anywhere along the tract. Bacilli found about port of entry, in edematous connective tissue, and in blood capillaries.

**Bubonic Plague.**—Petechial and larger ecchymoses in skin, mucous and serous membranes, boils and erysipelatous dermatitis, primary carbuncle at point of infection, secondary ones elsewhere. Hyperemia of spleen and kidneys, pneumonia and red infarcts of lungs. Chief lesions in lymph vessels: superficial nodes swollen with edema and bleeding in surrounding tissues; later, suppuration and external perforation of the nodes; commonest affected, inguinal, crural, axillary, cervical, the deeper ones may be a little affected. Bacillus in blood, abscesses and organs.

**Malaria.**—Spleen very large, hyperemia and hyperplasia at first, induration and pigmentation in chronic forms, rupture may occur in former condition with hemorrhage into peritoneum; liver swollen and hyperemic, pigment granules in and about capillaries; in some cases miliary collections of leucocytes, epithelial cells and pigment with fibrosis; kidney pigmented, epithelia degenerated, capillaries may contain plasmodium. Melanemic pigment also in bone marrow and brain.

**Morbilli.**—The skin lesions may have disappeared. Exudative inflammations of respiratory tract, bronchitis and pneumonia, commonest complication and cause of death. Hemorrhages in various surfaces in very severe forms. Cloudy swelling of viscera.

**Pyemia.**— Results of distribution of pyogenic organisms through the blood, with suppuration in joints and serous cavities, abscesses in viscera and muscles; but these lesions may be limited to a few organs, as the spleen and kidneys. Various degenerations of the visceral epithelium and lesions of complicating diseases, typhoid and scarlet fever, cholera and puerperal infection. The original focus of pus may be discovered, as otitis media, phlebitis in a superficial vein, etc. Post-mortem changes occur rapidly, icterus is common, the blood is fluid and brownish-red, rigor mortis may not be well developed.

**Rabies.**—Rigor mortis marked, face may be cyanotic, the wound which was the point of infection may not be found, or a scar firm and apparently normal. In recent cases the lymph nodes near the wound may be edematous and hyperemic. The meninges of cord and brain may be very hyperemic, as also the brain tissue; small hemorrhages may occur in the central nervous organs and extravasations about the origin of the pneumogastrics have been found. The pharyngeal mucosa is congested and the tonsils swollen; alimentary mucosa may be swollen, with punctate hemorrhages. The same may occur in the respiratory passages with inspiration pneumonia from dysphagia. Liver and spleen hyperemic with parenchymatous degeneration.

**Relapsing Fever.**—Spleen strongly swollen and hyperemic, may be ruptured, dark colored and soft; may be red infarcts. All other organs and voluntary muscles show acute parenchymatous degeneration; fatty changes in the heart may be marked. Intestinal canal shows hyperplasia of

lymphoid tissues. Organism in blood and spleen for hours after death.

**Scarlatina.**—Skin pale, desquamating in scales or in large epidermal leaves, may form casts of fingers. Otitis media, acute nephritis, hemorrhages in skin and membranes, meningitis and other complicating lesions may be present, with edema of face and legs.

**Septicemia.**—Putrefaction rapid, blood fluid and thin, hemorrhages on serous and mucous surfaces, cloudy swelling of organs and fatty degeneration. About the source of infection thrombosis and gangrene may occur or a purulent focus may be found. Various pyogenic organisms may be recovered from the heart's blood, exudate and organs, but many cases give negative results.

**Typhus Fever.**—Emaciation, gray color of surface, eruption not found, small hemorrhages in skin as small bluish-red spots over the whole body or chiefly the lower extremities; these may be merely pigmented spots. Rigor mortis marked but disappears early, putrefaction rapid, muscles brown and dry with waxy degeneration at times, hyperemia of meninges; spleen swollen, red and soft, fatty degeneration of heart and renal epithelium and liver cells; gall-bladder contains little thick and dark bile. Inflammatory changes in respiratory and alimentary mucosa, bronchitis, pneumonia, gastro-enteritis, etc.

**Variola.**—The eruption persists after death and may be found in any stage, other lesions are those of high fever and complications. The cystosporidia may be recovered from the skin lesions.

**Yellow Fever.**—Rigor mortis well marked and appears early, muscles dark and dry, skin yellow or very dark yellow green, subserous hemorrhages in lungs and heart, blood may be thin and fluid. Gastric mucosa strongly congested and swollen, hemorrhages into the membrane and in the cavity are common; the blood dark and thick (coffee

grounds); in the upper part of the small intestine similar lesions may be found, in the colon dysenteric necrosis may occur. Liver swollen, or moderately decreased, soft, color varies from dark red to light yellow with bile staining; gall-bladder contains a small amount of dark thick bile. Spleen may be small. Kidneys show acute nephritis, often hemorrhagic.

# INDEX.